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AUTHORS ALONE ARE RESPONSIBLE FOR OPINIONS EXPRESSED IN THEIR CONTRIBUTIONS

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BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

DECEMBER 1939

ADDRESS OF WELCOME
TWELFTH GRADUATE FORTNIGHT

MALCOLM GOODRIDGE

It is with a very real sense of pleasure and satisfaction that I extend to you the hearty welcome of the Academy of Medicine on this occasion. One of the objectives of the founders of the Academy, nearly one hundred years ago, was "The Cultivation and Advancement of the Science." With the founding of the Annual Graduate Fortnight, eleven years ago, we made a distinct contribution to the original aims of our forefathers.

I have heard the objection raised that postgraduate teaching is the function of the medical schools, and that in a short two weeks one could hardly do more than obtain some knowledge of the nomenclature of the subject under discussion.

I differ from those who hold such views. The New York Academy of Medicine is, first and foremost, an educational institution. The term, education, implies the acquisition as well as the imparting of knowledge; and it is the education we give ourselves which is the most valuable. If we are to read intelligently, we must understand the language we are reading.

I could not be convinced that the lectures, clinics, and exhibits ar-

ranged for previous Graduate Fortnights have not stimulated to further investigation those who have participated in its programs.

Tonight, we shall inaugurate our Twelfth Graduate Fortnight. The subject for discussion, this year, is, as you know, "The Endocrine Glands and their Disorders,"—a subject of great interest to almost every phase of medical practice. Indeed, the surgeon has made some of the most important contributions to our knowledge of the physiology and pathology of these glands.

The existence of many of the glands which we are about to discuss was known to ancient writers, and much of the groundwork of our present-day knowledge of endocrinology was laid in the nineteenth century. Nevertheless, our present-day conception of the subject is almost entirely a creation of the twentieth century. I mention this because it seems to me to emphasize the importance of this type of post-graduate teaching.

This year, you will note, we have added round table discussions to our program. You will find, in reading the names of the chairmen and leaders of these conferences, a sufficient guarantee of their potential value.

We are under great obligation to those men who are adding so greatly to the success of this Fortnight, by the contribution of so much of their time to the clinics, lectures, and round table discussions; and to the Committee on Medical Education, its subcommittee, and its executive staff, who have given so much of themselves, in terms of thought, time, and labor, in order that you might have a full measure of satisfaction during your attendance at the various exercises to be included in this Fortnight.

In closing, I hope I have made it plain that you will find a very warm welcome awaiting you at any of the clinics, round table discussions, and lectures you may desire to attend.

HYPOTHALAMIC-PITUITARY SYNDROMES*

LEOPOLD LICHTWITZ

THE hypothalamus is a central station in the autonomic nervous system for the control and regulation of vegetative functions. By its manifold activities the hypothalamus helps to maintain a constant internal environment. The conception of a constant internal environment we owe largely to the genius of Claude Bernard. The functional role of the hypothalamus in preserving the equilibrium has been well summed up by J. Barcroft,[1] who states "The physiology of the hypothalamus is the physiology of the internal environment."

The constancy of the internal environment depends upon a multitude of chemical and physical processes, such as secretions and excretions and their underlying metabolic requirements. Since metabolism is closely connected with endocrine secretion, regulation of vegetative functions must have a nervous as well as endocrinal character. It behooves us to understand the mechanism of this nervous and glandular coöperation.

The hormones, the powerful agents of the endocrine system, act in a definite order. This plan is carried out through the hypothalamic control of their production and release from the respective glands. The hypothalamus also plays a part in determining the degree of response to these hormones on the part of tissues and organs. The best known example of this type of hypothalamic control is the resistance to insulin in a diabetes originating from a hypothalamic lesion.

The hypothalamus responds to a large number of stimuli, such as temperature, osmotic pressure, pH; and is itself influenced by hormones. According to H. H. Meyer,[2] for example, the chief action of thyroxin is exerted upon the hypothalamus. In all probability the retarding influence of a number of endocrine glands upon the anterior pituitary is mediated by the hypothalamus.

The hypothalamus lies below the level of the thalamus, in the lateral wall and in the floor of the third ventricle from the posterior border

* Read October 24, 1939 at the Twelfth Graduate Fortnight of The New York Academy of Medicine.

of the optic chiasm dorsal, including the mammillary bodies. The posterior lobe of the pituitary may be considered a part of the hypothalamus; it develops from the floor of the third ventricle and as an avantguard brings the ectodermal anterior lobe into close contact with the hypothalamus. Thus anatomy and development indicate an intimate functional relationship between the hypothalamus and the pituitary.

The posterior pituitary lobe and the tuberal region of the hypothalamus (*Zwischenhirndruese*) are the sources of various hormones. Whether they are produced within the pituicytes which represent modified ganglion cells, or in the epithelial sheaths covering the posterior lobe and the tuber cinereum, is a matter under discussion.

The pituitary-hypothalamic complex is responsible for a large number of symptoms, syndromes, and well-defined disease entities. Since the secretion of the anterior lobe rests under the command of the hypothalamus, it is practically impossible to determine which function or lesion is purely hypothalamic or purely pituitary in origin. The following table shows the chief functions depending upon hypothalamic-pituitary activity:

TABLE I

FUNCTIONS DEPENDING UPON HYPOTHALAMIC-PITUITARY ACTIVITY

General metabolism
Carbohydrate metabolism
Fat metabolism and distribution of fat
Water metabolism (renal activity, sweating)
Thirst
Hunger and appetite
Growth and trophisms
Sexual development, maturation and activity
Cardiovascular activity (cardiac rhythm, blood pressure, vasomotor balance, circulating blood volume)
Gastrointestinal activity (secretions, tonus, peristalsis)
Formation of erythrocytes, leukocytes, thrombocytes and plasma proteins
Regulation of body temperature
Sleep (hypothalamic only)

In order to avoid false deductions, it must be borne in mind that in this part of the central nervous system the anatomical localization of a lesion does not necessarily mean localization of a function (H. Jackson,[3] Lhermitte[4]). The nuclear masses in the hypothalamus do not always represent well-defined centers by which isolated functions are controlled.

TABLE II

DISORDERS OF HYPOTHALAMIC-PITUITARY ORIGIN

High BMR	Low BMR	
Diabetes mellitus	Hypoglycemia	
Diabetes renalis		
Adiposity	Wasting (Cachexia)	
Lipodystrophy		
Fever	Hypothermia	Poikilothermia
Polyuria	Oliguria	
Diabetes insipidus		
Gigantism	Dwarfism	
Insomnia	Somnolence	
Pubertas precox	Delay and regression of sex development	
Arterial hypertension	Arterial hypotension	Vasomotor instability
Excessive salivation	Diminished salivation	
Gastric superacidity	Gastric subacidity	
	Achylia gastrica	
	Gastric-duodenal ulcers	
	Anomalies of gastrointestinal tonicity	
Polycythemia	Anemia	
Leukocytosis	Agranulocytosis	
Eosinophilia		
Osteoporosis	Eburnation	
	Arthritis	
Hirsutism	Alopecia	

The many pathological features enumerated in Table II may be grouped together into syndromes or well-defined diseases.

This rather imposing list is characterized by the large number of plus-minus variations, thus affirming the regulatory capacity of the hypothalamus.

The hypothalamus constitutes an essential instrument for emotional expression, normally restrained by cortical control. When in hypothalamic disorders cortical control is weakened or lost, emotional instability and abnormal behavior come to the fore. Emotional hypothalamic attacks are certainly more frequent than corresponds with the instances reported in the literature.

Hypothalamic-pituitary syndromes are brought on by four chief causes: Inherited or congenital defects, inflammation, trauma, and tumor.

Heredity plays an important role in the production of diabetes insipidus and of Froehlich's syndrome, the dystrophia adiposogenitalis. Encephalitis caused not only by influenza but all infectious diseases, and

also vaccination are of great etiological importance. Trauma and also surgical injury have been reported to be the cause in a number of cases. Leukemic infiltrations, Boeck's sarcoid, lymphogranulomatosis and xanthomatosis as well as primary or metastatic tumors produce the syndromes either by direct destruction of the tissues of the hypothalamo-pituitary territory or by pressure exercised directly or by an internal hydrocephalus.

The allotted time will not permit consideration of all the hypothalamic-pituitary syndromes. However, by discussing a few of them, namely, diabetes insipidus, abnormal ratio of growth with infantilism (infantile gigantism), and Froehlich's syndrome we may gain a general understanding of the underlying mechanism and of the possibilities of therapy. We may start with diabetes insipidus.

Diabetes Insipidus

Diabetes insipidus originates from a disorder in the anterior hypothalamus and is controllable by the pituitary antidiuretic hormone, which is found and probably produced not only in the posterior lobe but also in the tuberal region of the hypothalamus. Therefore, total hypophysectomy need not eradicate the hormone and does not produce diabetes insipidus. Two factors underlie the genesis of diabetes insipidus, namely, absence of the antidiuretic hormone or failure of response to this hormone. Thus diabetes insipidus may exist in spite of a perfectly normal pituitary gland. It is generally agreed that physiologically the antidiuretic hormone acts on the hypothalamus itself. Of course, there is no doubt that experimentally and therapeutically the hormone is able to produce oliguria by direct action on the kidney proper and on capillaries generally. This universal action does not contravert anatomical, experimental and therapeutic evidence as to the direct influence of the antidiuretic hormone on the hypothalamus.

The nerve elements responsible for the control of the diuresis are well known. The paraventricular and supraoptic nuclei in the anterior hypothalamus are linked to the posterior lobe by the supraoptico-hypophyseal tract, abundant fibers of which take up a direct contact with the specific cells in the pars tuberalis and media. Another fiber tract runs between the tuberal nuclei and the posterior pituitary. These nuclei and the posterior lobe represent a functional unit. Destruction of the nuclei is followed by atrophy of the posterior lobe and destruc-

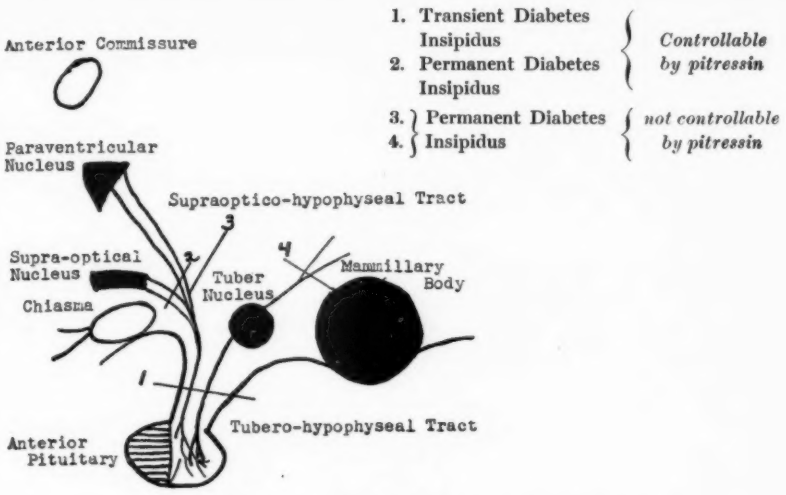

Fig. 1—The pituitary-hypothalamic control of diuresis.

tion or removal of the posterior lobe leads to atrophy of the cells of the nuclei. The destruction of the supraoptico-hypophyseal tract causes degeneration of the hypothalamic nuclei as well as of the posterior pituitary (Fisher, Ingram and Ransom[5]). Bilateral lesions within this system cause diabetes insipidus.

The investigations of Labbé and Azérad,[6] Dreyfus[7] and Biggart[8] indicate that the tuberal nuclei and the nerve tract running from these nuclei toward the mammillary bodies (tractus tuberalis descendens) possess a special importance in that lesions involving this tract render the diabetes insipidus refractory to the antidiuretic hormone.

The functional significance of diabetes insipidus lies in the fact that one of the most important renal functions is disturbed, namely, the ability of the kidney to retain water. In diabetes insipidus the excretory renal requirements cannot be fulfilled by means of a normal or small quantity of water. It is now well established that the extreme thirst of diabetes insipidus is not primary but that it is secondary to the uncontrolled diuresis.

Three types of diabetes insipidus may be differentiated. The first does not show any other symptom than polyuria. In these cases during a period of oliguria, easily enforced by the injection of the antidiuretic

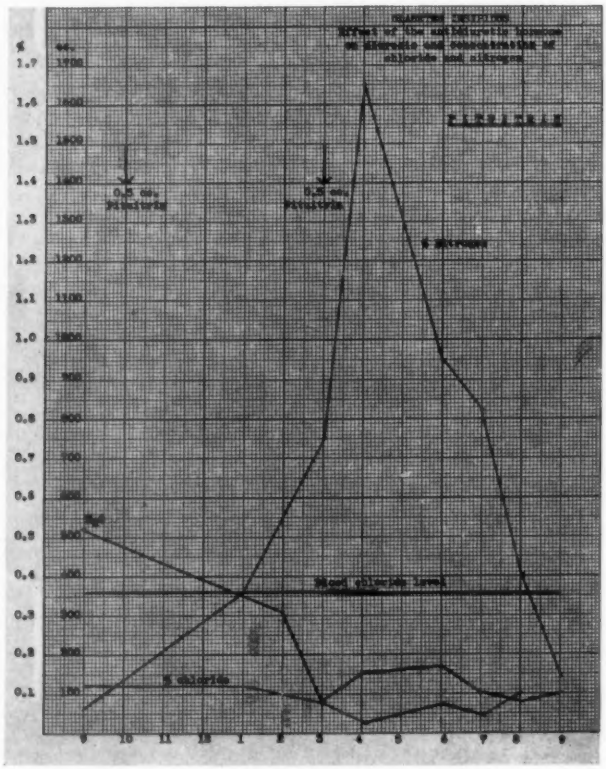

CHART I—DIABETES INSIPIDUS. Effect of the antidiuretic hormone on diuresis and concentration of chloride and nitrogen.

hormone, the kidneys reveal normal concentrating capacity. A second group is characterized by polyuria and failure in concentrating ability in respect to chlorides, bicarbonates and basic elements. Even in extreme oliguria the urinary concentration of chlorides remains unaltered—it may be as low as 100 mg. per 100 cc.—or at best it rises to the blood chloride level. Finally, there is a third type in which the polyuria decreases to inconspicuous figures, e.g., 2000 cc., but the failure to concentrate remains. This points to a hypothalamic apparatus of the concentrating power of the kidneys and its independence from the diuresis of water.

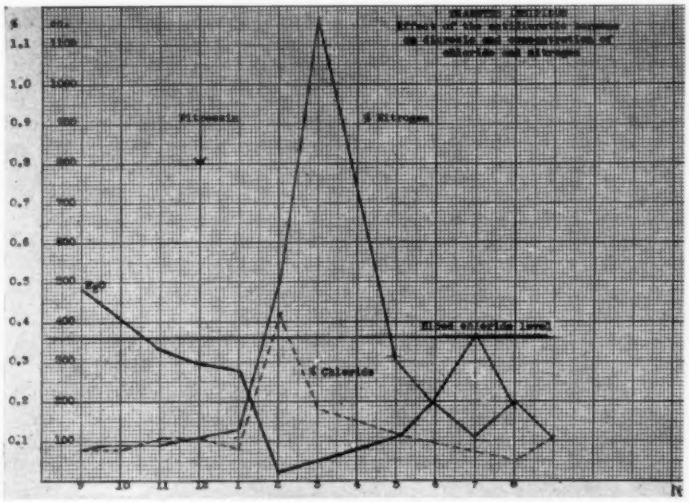

CHART II—DIABETES INSIPIDUS. Effect of the antidiuretic hormone on diuresis and concentration of chloride and nitrogen.

Diabetes insipidus may be a permanent or sporadic state, or may vary in degree, or may cease completely, just as is the case in diabetes mellitus of hypothalamic origin. In fact, even when caused by a most substantial pathological lesion, such as a metastatic cancer or a leukemic infiltration, the abnormality may disappear. This fact corresponds with experimental observations, according to which destruction of the posterior lobe or dissection of the pituitary stalk causes an increased secretory activity of the tuberal part of the hypothalamus and, therefore, a polyuria which lasts very briefly. The failure of the concentrating capacity also may be transitory in character.

Hann[9] has advocated the idea that diabetes insipidus does not develop in the absence of the anterior pituitary, which, he believes, produces a diuretic hormone. There is no satisfactory proof of the validity of this conception. However, it seems likely that inactivity of the thyroid gland, which necessarily follows the absence of thyreotropic hormone, may prevent or counteract the polyuria. Thus after total hypophysectomy diabetes insipidus can be provoked by the administration of thyroid extract. According to a case report by L. Strauss,[10] diabetes insipidus

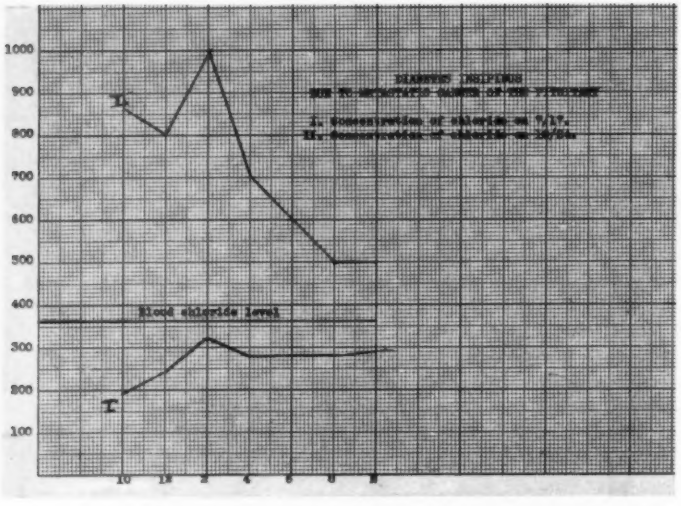

CHART III—DIABETES INSIPIDUS. Due to metastatic cancer of the pituitary. I, Concentration of chloride on 7/17. II, Concentration of chloride on 10/84.

disappeared after the development of myxedema, and T. Findley, Jr.[11] has found an increase of the effect of pitressin after thyroidectomy. These observations have led to an attempt to control diabetes insipidus by thyroidectomy. Good results have been reported in a few cases.

The functional character of diabetes insipidus is evidenced by the disappearance of the polyuria during fever, sleep, and anesthesia—conditions which temporarily change the activity of the hypothalamus.

It is well known that during sleep all the secretory and excretory processes are depressed. When this coöperation between the mechanism responsible for sleep and the control for secretory and excretory processes fails, nocturia, nocturnal salivation, night sweats and nocturnal gastrosuccorrhea result.

Etiologically we may differentiate as a separate group the idiopathic diabetes insipidus, which is frequently hereditary. In the famous family investigated by Adolf Weil,[12] of Heidelberg, and Alfred Weil,[13] of New York, 35 of 220 members in five generations suffered from the disease which in this instance happened to be a dominant hereditary character. There seem to be no records of anatomical studies on the

hypothalamus and the pituitary in idiopathic diabetes insipidus. However, even though structural alterations should not be detectable, the frequent coincidence of diabetes insipidus with other hypothalamic disorders points to the hypothalamic origin.

In the majority of the cases polyuria is the only manifestation of the hypothalamic disorder and may last throughout life, the span of which is not shortened. After the age of fifty the disturbance frequently becomes less troublesome. Pregnancy has a definite influence, either decreasing or increasing the polyuria. Rest is beneficial. The prognosis does not depend on the degree of the polyuria, even when so excessive as 43 liters a day, as in a case reported by Trousseau.

Non-idiopathic diabetes insipidus is chiefly secondary to tumors and inflammatory pathology. Particularly in children infectious diseases, such as measles, scarlet fever, pertussis, diphtheria, chickenpox, mumps, erysipelas, influenza, and also vaccination may bring on a persistent diabetes insipidus. Xanthomatosis causes diabetes insipidus in 60 per cent and pellagra in 25 per cent of the patients.

The therapy may be considered from the viewpoint of the ways and means of influencing the hypothalamus generally. This principle may be exemplified on the basis of methods which influence heat regulation and at the same time water elimination.

The Viennese school of E. P. Pick[14] has established the antidiuretic effect of antipyretics. Particularly aminopyrine has been used successfully in diabetes insipidus and has been seen to interfere with mercury diuretics. We have used aminopyrine against nocturia in cases of chronic mesencephalitis with good results, as shown in Table III.

It has been observed that in diabetes insipidus the polyuria may become diminished or even disappear during a period of fever. Fever induced by foreign proteins, or other substances, may have the same effect. Here the rise in the temperature originates in that part of the temperature center which controls the production of heat. The rise of temperature brought on by hot baths, the fever machine, or other means, is quite different in its mechanism, for here the apparatus designed to get rid of heat becomes active. The diuresis may be diminished by either mechanism or by both.

The chief agent for the treatment of diabetes insipidus is the antidiuretic hormone. It is available as the extract of the posterior and of the intermediary pituitary. Pitressin applied subcutaneously may produce

TABLE III

EFFECT OF AMINOPYRINE ON NOCTURIA

CASE	TOTAL URINE CC.	REDUCTION OF THE DIURESIS [PER CENT]	URINE DAY	URINE NIGHT	NOCTURIA IN PERCENTAGE OF TOTAL	AMINOPYRINE
I	2570		770	1800	70	
	1720	33	1070	650	30	+ +
II	2130		530	1600	75	
	1495	30	845	650	43	+ +
III	2360		860	1500	63	
	1050	56	870	180	17	+ +

oliguria for a period of 4 to 6 hours but sometimes for 24 or even 48 hours. In a small number of cases thirst is a hypothalamic symptom independent from the polyuria and not influenced by the antidiuretic hormone. In such cases treatment with antidiuretic hormone is contraindicated because the patient, continuing to take in large quantities of fluid, but unable to excrete corresponding amounts of urine, may become dangerously ill from a syndrome which has been termed "water intoxication." In another group of cases the vasomotor effect of the posterior lobe extract may cause considerable discomfort. In that event an extract of the intermediary lobe may be tried. In 1922, H. L. Blumgart[15] introduced the intranasal application of the antidiuretic hormone. This method is more effective and certainly more convenient than the subcutaneous route, provided the patient's snuffing technique is good and he can stand it without getting nasal catarrh. The nasal application of 50 mgms. of the extract is sufficient in most cases. The smallest effectual dose should be established and administered as frequently or as rarely as necessary.

According to reports in the literature, follicular hormone has been helpful in a number of cases. This effect is creditable since we know that this hormone and others counteract the activity of the anterior lobe acting via the hypothalamus. In diabetes insipidus it seems essential to depress the anterior lobe and consequently the use of anterior pituitary hormones and particularly of the thyreotropic hormone is contraindicated. This also applies to the thyroid hormone because of its diuretic

effect. An attempt may be made to depress the thyroid secretion by administering diiodotyrosine. The use of sedatives is to be recommended and may be combined with atropine and aminopyrine, particularly in cases resistant to the antidiuretic hormone. Antisyphilitic treatment will be successful in suitable cases. Removal of 8 to 15 cc. of spinal fluid by spinal puncture is recommended by Herrick and may be of value particularly in cases with increased intraventricular pressure.

Dystrophia Adiposogenitalis

Dystrophia adiposogenitalis, Froehlich's syndrome, is another pituitary-hypothalamic syndrome of major importance. It is characterized by obesity and failure or delay of sexual development. There is in New York City a particularly large number of individuals of this type, who show a strong hereditary and familial trend. Groups of human beings—I purposely avoid the misinterpreted and criminally applied term race—in which there is a tendency to obesity, as for instance in the peoples originating from Southern and Southeastern Europe and Asia Minor, seem to produce a relatively larger number of individuals of the Froehlich type.

It should be borne in mind that height and weight are stigmata of pituitary-hypothalamic origin and that the change in height which has taken place in the last twenty-five years, points to an evolutionary change in pituitary-hypothalamic activity. This last period has produced a larger number of tall individuals with long limbs and a relatively short torso, on which is perched a small head with a long face. The disproportionate growth of the limbs is caused by the delay in sex maturation. This type of abnormal ratio of growth with infantilism (infantile gigantism) represents a pituitary-hypothalamic anomaly linked to the eunuchoid type. Its somatic characteristics are paralleled by a definite mental pattern. These individuals are emotional rather than rational and are governed by sentiment rather than by reason. They have little stability, lack self-confidence and dread to assume responsibility or to face the world alone. Hence they are easily herded by a man who claims to be their leader, holding out to them prospects of green pastures and greatness. It is interesting that in the present Germany this infantile gigantism is portrayed as the ideal of manhood and knighthood in the statue of "Siegfried." (Fig. 2)

Dystrophia adiposogenitalis is usually congenital. The endocrine

Fig. 2—"Siegfried" statue in present day Germany shows the characteristics of infantile gigantism.

and nervous origin of the outstanding symptoms–adiposity and sexual retardation–have been clarified in recent years. According to P. E. Smith,[16] destruction of the anterior pituitary causes atrophy of the gonads but not adiposity. Obesity results from basophile and chromophile pituitary adenoma. Cushing[17] found rapid increase in weight with amenorrhoea in 60 per cent of females with chromophile adenoma before pressure on the optic chiasm became apparent. However, obesity of hypothalamic origin is equally well known ever since O. Marburg[18] described the first incident in a case of internal hydrocephalus (1907).

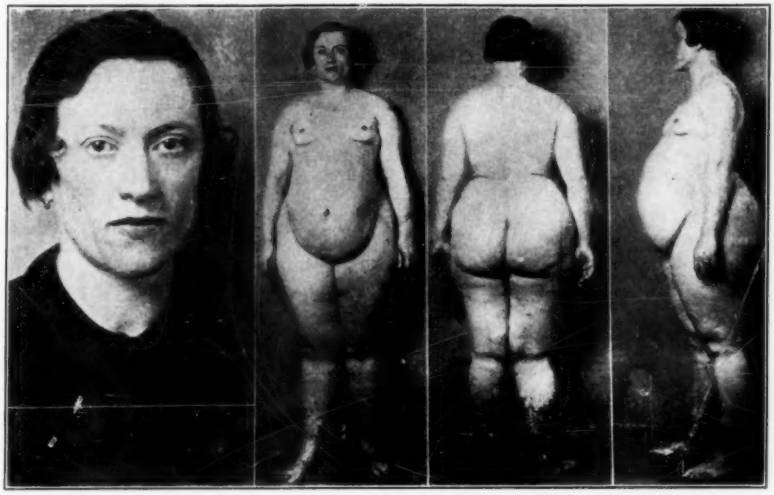

Fig. 3—Lipodystrophia.

Smith has demonstrated in experiments that hypothalamic damage produces obesity without gonadal changes. Pituitary and hypothalamic obesity have identical features and are characterized by the deposition of fat on the trunk, the lower part of the abdomen and the proximal parts of the limbs, whereas the forearms and the calves remain slender. In a few cases the distribution of the fat takes a different form and may result in the so-called lipodystrophia with masses of fat below the girdle and emaciation of the upper parts, particularly the face, where every trace of fat may disappear. We also have seen a case with an accumulation of fat on the neck and abdomen and complete fat atrophy on the extremities.

The pituitary-hypothalamic complex causes obesity not by the failure of a hormone responsible for the catabolism of fat—it is even doubtful whether such a "fat hormone" exists—but by its influence on the fat cells themselves. The combination of obesity or lipomatosis with fat atrophy in definite areas indicates the general neuro-endocrine influence, which renders the fat tissue lipophilic, attracting fat, as well as lipophobic, barring fat, accentuating thus in the females the fat distribution characteristic of the female sex and feminizing the external appearance of males. This is most conspicuous in those instances in which the dis-

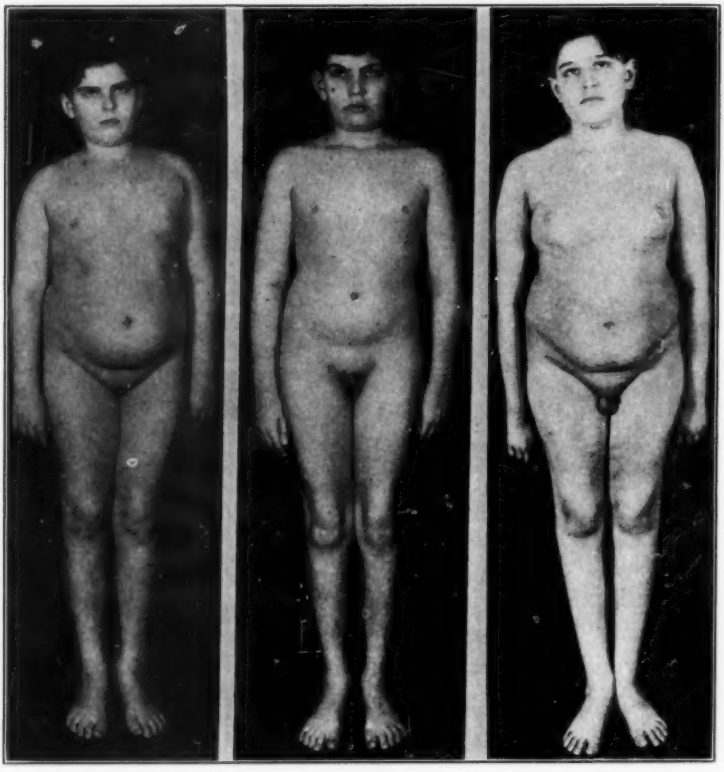

Fig. 4—Three cases of Froehlich's syndrome.

tribution of fat is altered without apparent obesity and fat accumulates above the hipbones, as in the case of a boy with infantile gigantism.

Differentiation between the pituitary and the hypothalamic origin of obesity combined with hyposexualism—if it can be said to be an actual difference at all—depends upon variations in growth. When the pituitary influence predominates, retardation of growth and pituitary dwarfism may result. When the hypothalamic influence is prevalent, growth continues and, owing to the relationship between sex maturation on the one hand and ossification and closure of the epiphyses on the other, leads to the tall eunuchoid type or infantile gigantism.

Children and adolescents with the Froehlich syndrome look very

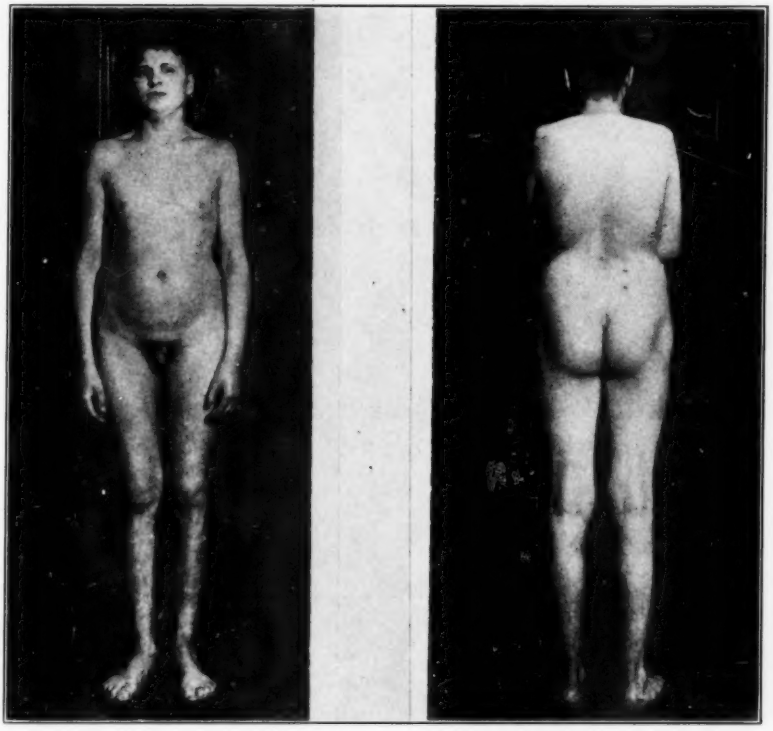

Fig. 5—Infantile gigantism.

much alike, as if belonging to the same family tree, and also have marked similarities in character, temperament and behavior. They retain the infantile habitus over long and are slow in developing a definite individuality. Girls not infrequently develop an inferiority complex and a rather violent desire to normalize their appearance.

This, however, is rather difficult to accomplish. The basic part of the obesity scarcely responds to such dietary restrictions, as are suitable and applicable during the growing stage, when used over a longer period of time. However, not infrequently reduction of weight takes place spontaneously with the onset of sexual maturation. The additional adiposity resulting from overeating can be removed. Overeating in this type is not so much due to a blamable overindulgence as to episodes of hypoglycemia with its feeling of stomach emptiness, acute hunger,

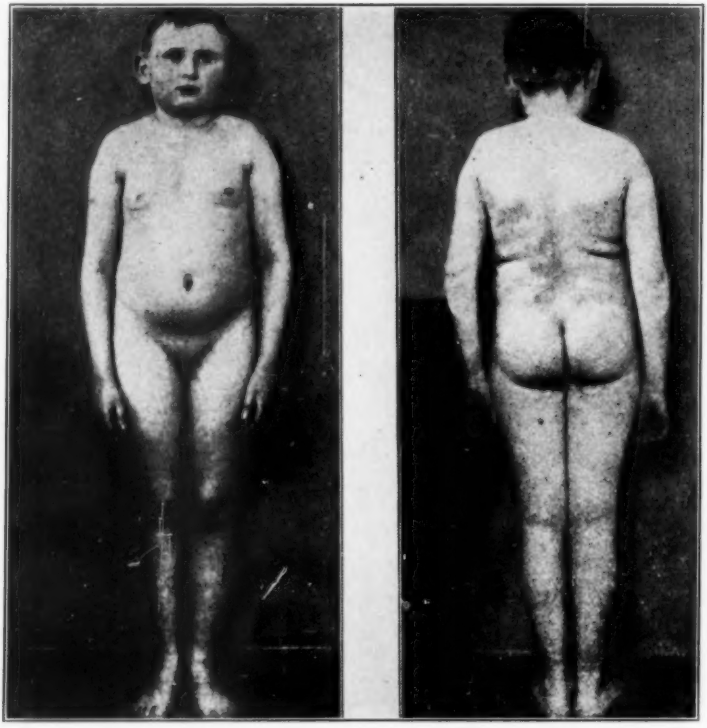

Fig. 6—Pituitary dwarfism.

weakness, craving for food, especially sweets. In such cases the dietary management of the hypoglycemia should be resorted to. During the period of growth, as a rule, a diet almost sufficient in caloric value, rich in proteins and otherwise consisting of fruits, vegetables, particularly in a raw state, with a limited amount of bread and cereals and very poor in fat, is advisable. The administration of thyroid extract is frequently indicated and a dose just below the individual tolerance should be given. Gonadotropic hormone is expedient in order to stimulate the sexual development. This therapy has been successful in a number of cases but is by no means always a panacea. In the fortunate individuals the descent and growth of the testicles can be induced. In the majority of cases sexual maturation sets in spontaneously during the age of adolescence. Thus it occurs that a man with the history and some earmarks of the

Froehlich syndrome may have a son of the same type.

It may be worthwhile mentioning that children with Froehlich syndrome apparently are particularly susceptible to infectious diseases and often are stricken with rheumatic fever. This may be interpreted from the viewpoint that these individuals are more infantile than normal children and thus more susceptible to the infectious diseases of childhood. Or it may point to the relationship of the pituitary-hypothalamic apparatus to the mechanism of defense and immunization.

In conclusion I might emphasize that the relationship between the nervous system and the endocrinal glands, culminating in the hypothalamic-pituitary complex, represents a central point from which the many parts of the medical science are visible; some of them at close range, others still in the far distance, but all of them recognizable as integral parts of the indivisible entity, Medicine.

REFERENCES

1. Barcroft, J. *Features in the architecture of physiological function.* Cambridge [Eng.], University Press, 1934.
2. Meyer, H. H. Zur Theorie der Schilddrüsenwirkungen, *Deutsche med. Wchnschr.*, 1931, *57:* 1531.
3. Jackson, J. H. Remarks on evolution and dissolution of the nervous system. *J. Ment. Sc.*, 1887, *33:* 25; also in his *Selected Writings.* London, Hodder & Stoughton, 1932, v. *2,* p. 80.
4. Lhermitte, J. Les syndromes anatomocliniques dépendant de l'appareil végétatif hypothalamique, *Rev. neurol.*, 1934, *1:* 920.
5. Fisher, C., Ingram, W. R. and Ranson, S. W. *Diabetes insipidus and the neurohormonal control of water balance.* Ann Arbor, Mich., Edwards Bros., 1938.
6. Labbé, H. and Azérad, E. Le diabète insipide, *Ann. de med.*, 1926, *20:* 392.
7. Dreyfus, G. *Le diabète insipide.* Paris, Doin, 1931.
8. Biggart, J. H. Diabetes insipidus; the site of formation of the anti-diuretic hormone, *Edinburgh M. J.*, 1936, *43:* 417; and The anatomical basis for resistance to pituitrin in diabetes insipidus, *J. Path. & Bact.*, 1937, *44:* 305.
9. Hann, F. von. Über die Bedeutung der Hypophysenveränderungen bei Diabetes insipidus, *Frankfurt. Ztschr. f. Path.*, 1918, *21:* 337.
10. Strauss, L. Uebergang eines Falles von Diabetes insipidus in Myxödem, *Deutsche med. Wchnschr.*, 1920, *46:* 939.
11. Findley, T., Jr. Thyroid-pituitary relationship in diabetes insipidus, *Ann. Int. Med.*, 1937, *11:* 701.
12. Weil, A. Ueber die hereditäre Form des Diabetes insipidus. *Virchows Arch. f. path. Anat.*, 1884, *95:* 70.
13. Weil, A. Über de hereditäre Form des Diabetes insipidus, *Deutsche Arch. f. klin. Med.*, 1908, *93:* 180.
14. Pick, E. P. Pharmakologie des vegetativen Nervensystems, *Deutsche Ztschr. f. Nervenh.*, 1928, *106:* 238.
15. Blumgart, H. L. Antidiuretic effect of pituitary extract applied intranasally in a case of diabetes insipidus, *Arch. Int. Med.*, 1922, *29:* 508.
16. Smith, P. E. Disorders induced by injury to the pituitary and the hypothalamus, *J. Nerv. & Ment. Dis.*, 1931, *74:* 56.
17. Cushing, H. W. *Papers relating to the pituitary body, hypothalamus and parasympathetic nervous system.* Springfield, Ill., Thomas, 1932.
18. Marburg, O. Zur Frage der Adipositas universalis bei Hirntumoren, *Wien. med. Wchnschr.* 1907, *57:* 2512.

PHYSIOLOGY AND PRINCIPAL INTERRELATIONS OF THE THYROID GLAND*

DAVID MARINE

ANATOMY

THE thyroid gland of vertebrates in its normal or colloid stage morphologically suggests a storage gland, and in its hyperplastic stage a very active secreting gland. It is one of the most labile tissues in the body—capable of undergoing detectable morphological changes within a few hours. Because of this rapid and wide range of anatomical changes we are provided with a very delicate (at present too delicate for clinical use) anatomical measure of functional variations. This series of morphological changes may be designated as the anatomical cycle and consists of (1) hypertrophic or hyperplastic, (2) colloid or resting, and (3) atrophic stages. The actively hypertrophic or hyperplastic stage according to my belief is the initial stage of goiter formation. It indicates stimulation and increased functional activity of the cells but not necessarily an increased production of the thyroid hormone. This stage, so far as it is at present known, is brought about by the thyrotropic factor of the anterior pituitary. The colloid stage represents the return of the hyperplastic stage to its functionally normal or quiescent state, and the atrophic stage represents the permanently exhausted state of the thyroid. There is at present no basis for assuming that the morphological cycles in endemic goiter, in Graves' disease, in compensatory hypertrophy following partial removal or the hypertrophy following injections of anterior pituitary extract differ in any essential manner.

PHYSIOLOGY

Our knowledge of thyroid physiology began with Sir William Gull's recognition in 1874 of thyroid atrophy in the disease that bears his name. This was followed by the production by the Reverdin brothers (1882) and T. Kocher (1883) of a condition resembling Gull's disease following total thyroidectomy for the cure of goiter.

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In 1891 Murray cured a case of Gull's disease by injecting a glycerol emulsion of fresh sheep's thyroid and in 1892 Howitz, McKenzie and Fox independently demonstrated that dried or cooked thyroid was equally efficacious when administered orally. In 1895 Magnus-Levy, using the newly developed calorimeter, discovered that in Gull's disease the heat production was lowered as much as 40 per cent. Later work showed this lowering of metabolism was a typical effect of thyroidectomy in all mammals tested. The fall in metabolism usually begins in mammals between the fifth and seventh days after thyroidectomy, and reaches its lowest level in the rabbit between the twentieth and thirtieth days. In man it is said to reach its lowest level about the sixtieth day.

Magnus-Levy further demonstrated that the oral administration of desiccated thyroid substance raises the metabolic rate in cases of Gull's disease as well as in normal persons. These observations determine the principal function of the thyroid as we know it today. In 1912 Gudernatsch found that feeding thyroid to tadpoles caused metamorphosis in two to five days. This is still the most delicate test for the thyroid hormone. It was suggested that this effect on tadpoles might be due to its metabolism-raising effect, but work in recent years, especially with the dinitrophenols, shows that these substances greatly increase the metabolism of tadpoles and of myxedema patients without causing metamorphosis or therapeutically benefiting cases of Gull's disease. The thyroid hormone, therefore, has a specific action not exhibited by iodides nor by metabolism raising substances (adrenalin, dinitrophenol).

The thyroid is richly supplied with vasomotor nerves but the older view that its secretion was under specific nervous control has been abandoned. Cannon and his co-workers thought they had demonstrated such control by anastomosing the phrenic nerve with the distal end of the cervical sympathetic trunk (Langley operation). This work lacks confirmation. Manley and Marine demonstrated that multiple thyroid autotransplants located in widely different parts of the body anatomically respond similarly and simultaneously with the reactions going on in the intact portion of the thyroid. It was also shown that the growth of thyroid transplants was inversely proportional to the amount of thyroid gland removed. These observations indicated that the stimulus for increased functional activity was humoral and not nervous. Smith's and Allen's work on tadpoles demonstrated that this humoral factor was a

hormone (thyrotropic) from the anterior pituitary gland. Baumann and Hunt (1925) demonstrated that the thyroid gland was necessary for Rubner's specific dynamic action of ingested foods in rabbits. They found that it disappeared in thyroidectomized rabbits in from sixty to sixty-five days and could be restored by the administration of desiccated thyroid or thyroxine. Houssay working with dogs thought that hypophysectomy alone did not modify the specific dynamic action and that thyroidectomy did not entirely abolish it. The mode of action of thyroxine in increasing oxidations in the body is unknown. The stimulation is a very general one since it increases the oxidation of proteins, fats and carbohydrates in their normal proportions as indicated by the respiratory quotient. The opinion has been generally held for many years that the thyroid hormone brought about these increased oxidations by activating the various enzyme systems concerned. However, no specific proof has been produced despite the enormous work. It has been found that the catalase of the blood and liver is increased and the lipase is decreased by thyroid feeding. Thyroidectomy decreases the blood catalase. Rohrer first showed that the oxygen consumption of minced liver, kidney and muscle of thyroid fed rats was increased and Ahlgren demonstrated that minced muscle from thyroidectomized animals consumed less oxygen. Thyroxine added to normal tissues in vitro is without effect. Cannon and his co-workers have demonstrated that thyroxine was as effective in raising metabolism of sympathectomized cats as in normals. Thyroxine reduces the ascorbic acid and glutathione contents of the blood, indicating that more of these active agents are consumed when oxidation processes are increased.

We have recently reported an observation supporting the enzyme activation theory of thyroxine action. Marine and Rosen found that the administration of desiccated thyroid to rabbits greatly hastens the hydrolysis of testosterone propionate when this substance is injected in oil subcutaneously. Thyroidectomy was found greatly to reduce the urinary excretion of androgens when testosterone propionate was injected, but did not influence significantly the excretion of androgens when testosterone was injected.

There appears to be sufficient evidence to indicate that thyroxine is only the active chemical group of the true thyroid hormone. This was first indicated by the work of Reid Hunt (1923) who showed that thyroxine is less active than iodine equivalent amounts of desiccated

thyroid. Oswald has shown that thyroglobulin injected into the circulation causes an almost immediate increase in the heart rate while thyroxine increases the pulse rate only after a long latent period. More recently Cruz-Coke and others have shown that when thyroxine is incubated for forty-eight hours in homologous serum, then injected into rats, the latent period is reduced twenty-four to forty-eight hours. The work of Salter and Lerner also confirms the view that the physiological activity of desiccated thyroid is proportional to the total iodine rather than the thyroxine iodine.

Biochemistry

Coindet's demonstration (1820) that iodine was beneficial in the treatment of goiter made it possible quickly to establish that iodine was the active agent in burnt sponge, sea salt, and seaweed, which had been used beneficially for centuries in the treatment of goiter.

Attempts to demonstrate iodine in the thyroid failed until 1895 when Baumann reported that it was a normal constituent of the gland in mammals. Baumann showed that it was present in variable amounts as a stable organic compound and isolated a brownish powder (iodothyrin) by acid hydrolysis containing up to 10 per cent of iodine. Hutchinson showed that the iodine was contained in the colloid, and Oswald (1899) showed that the colloid was a globulin and introduced the terms thyroglobulin and iodothyroglobulin, since he also recognized that this globulin could be rich or poor in iodine. The globulin content is approximately the same whether the gland is in the colloid state or in the hyperplastic state. The maximum amount of iodine in the thyroid is about 1 mg. per gm. of fresh tissue and this occurs only in normal and colloid glands. The minimum amount is an inestimable trace and this occurs in the most marked degrees of hyperplasia. Between these extremes there are all gradations of iodine content. The normal human thyroid weighs approximately 20 to 25 gm. and may contain a maximum of 1 mg. of iodine per gm. but the average iodine content is about one half this amount (10 to 15 mg.). Iodine appears in the calf's thyroid as early as the third month of fetal life (Fenger). The surviving thyroid, both in vitro and in vivo, has a unique selective ability to take out and fix iodine reaching it through the blood or other circulating fluid. No other tissue has this capacity and so far as is known the thyroid is the only organ capable of elaborating the iodine containing hormone. Human blood normally

contains between 3 and 6 gamma per cent of iodine and possibly one-third of this is thyroxine iodine (Elmer). The older figures giving 10 to 15 gamma per cent are obviously too high (Baumann).

All efforts to utilize acid hydrolysis for the isolation of the active principle failed. Oswald tried barium hydroxide because Drechsel (1896) had successfully used this method in isolating diiodotyrosine from coral. Oswald failed to obtain the active fraction because, as Harington pointed out, he discarded the acid insoluble fraction with the barium sulphate. Hutchinson, Oswald and others tried peptic and tryptic digestions but failed. Kendall (1913) again undertook to use the method of alkaline hydrolysis and showed that the iodine became increasingly dialyzable through celloidin membranes when thyroid was carefully heated with dilute sodium hydroxide. In 1914 Kendall hydrolyzed thyroid with a 1 per cent sodium hydroxide in 90 per cent alcohol and was able to separate the organic iodine into two fractions: a) acid, insoluble and b) acid, soluble. Kendall showed that the acid insoluble fraction increased the metabolic rate like desiccated thyroid, while the acid soluble fraction did not. In 1916 Kendall announced the isolation of a crystalline compound (thyroxine) from the acid insoluble fraction containing approximately 65 per cent of iodine and which physiologically produced the same effects as desiccated thyroid.

The yields were very poor and his attempts to determine its empirical and structural formulas were unsuccessful. Nurnberg (1907), using Baumann's iodothyrin, attempted to ascertain the iodine holding organic group of thyroglobulin. He was unsuccessful, but certain reactions led him to suggest that the iodine was bound with tyrosine—probably as diiodotyrosine. In 1926 Harington greatly improved the method of extracting thyroxine from the thyroid by returning to the barium hydroxide method of Drechsel. He was able to accumulate sufficient quantities to determine its empirical formula as $C_{15}H_{11}O_4NI_4$, and that structurally it was composed of two molecules of diiodotyrosine, with the loss of one alpha amino-propionic acid side chain and the two benzene rings joined by an ether linkage. The organic nucleus of thyroxine Harington named thyronine. In 1927 Harington and Barger, and independently Dakin, synthesized thyroxine and showed that it had the same physiological effects as natural thyroxine. Harington further showed that the acid soluble iodine (part b of Kendall) was diiodotyrosine and identical with that found in coral and sponge. Foster (1929)

confirmed the presence of diiodotyrosine in the thyroid gland and was able to recover as much as 30 per cent of the total iodine as this compound. Harington found that approximately 60 per cent of the iodine of the thyroid is present as diiodotyrosine and 40 per cent as thyroxine. The proportion of these two compounds in the thyroid in relation to variations in the iodine store has not been carefully studied, but if it were found that they rose and fell together, it would be further evidence in favor of the view that the true thyroid hormone is a globulin containing both thyroxine and diiodotyrosine. It is known that the activity of desiccated thyroid is proportional to its iodine content rather than to its thyroxine content (Reid Hunt, Oswald, Salter and Lerner, Cruz-Coke).

In 1936 Ludwig and von Mutzenbecker obtained a substance chemically and physiologically identical with thyroxine by hydrolyzing iodinized casein with weak alkali and heat. This has been confirmed in this country by Foster and in England by Harington. Heretofore only diiodotyrosine had been obtained by hydrolyzing nonspecific iodinized proteins. The reactions which occur in the production of thyroxine from iodinized casein are not known. Ludwig and von Mutzenbecker suggested that iodine could oxidatively couple two molecules of diiodotyrosine with the loss of one side chain. Harington, however, thinks this is unlikely and suggests that possibly thyronine may exist in proteins rich in tyrosine-like casein. Thyroglobulin, however, according to analyses by Epstein, White, Cavett and others, is not an unusual protein as regards its tyrosine content.

Another constituent of the thyroid gland is bromine. This has long been known (1898) but little attention has been paid to its possible role in thyroid physiology until recently. The bromine content of the thyroid averages considerably higher than that of other tissues. Thus Neufeld found around 2 mg. per cent of bromine in normal human thyroids and 1 mg. per cent in the blood. The relation of the bromine content to thyroid structure, if any, has not been determined, and whether any ratio exists between iodine and bromine in the thyroid is likewise unknown. Bromine alone will not involute thyroid hyperplasia but according to Gaddum tetrabromthyronine has a slight thyroxine-like action. Baumann and myself have also confirmed the fact that the bromine content of the rabbit's thyroid is higher than the blood bromine. Moruzzi (1938) found that feeding sodium bromide in doses of .17 to .25 gm. per kg. daily to

dogs caused a progressive loss of iodine from the thyroid gland for the duration of the experiments—560 days. The bromine content rose abruptly during the first sixty days, then declined almost as rapidly. Rabbits' thyroids reacted similarly. There is some clinical evidence that bromine administered with iodine may be more beneficial in the treatment of goiter than iodine alone. No evidence exists at present to indicate that bromine, although constantly present, is of biological importance, but there are ample grounds for the further investigation of this question.

Interrelations

As the nature and importance of the interrelations of the endocrine glands becomes understood the conception of a purely thyroid disease correspondingly declines, and in my opinion the exact role of the thyroid in disease processes cannot be determined until these intricate interrelations are worked out. Considerable progress has been made in this field during the past twenty years and the following summary of some of these interrelations may be of interest because of their possible importance in clinical medicine.

Thyroid-Pituitary

It has been known for more than a century that persons and animals with large goiters have enlarged pituitary glands. Nièpce (1851) observed pituitaries in goitrous cretins weighing 2.4 gm. (normal, 0.5-0.7 gm.). Rogowitsch (1889) was the first to produce hypertrophy of the anterior pituitary in rabbits by thyroidectomy. This observation has generally been confirmed and the generalization may be made that in all states of severe thyroid insufficiency (cretinism and Gull's disease, endemic goiter) the anterior pituitary tends to undergo hypertrophy. In Graves' disease, on the other hand, the pituitary is usually normal or low normal in size. Histologically all the elements of the anterior pituitary appear hypertrophic and in the rabbit the most striking single feature is the degranulation of the eosinophilic cells. These granules may be promptly restored by the administration of thyroxine or desiccated thyroid. The physiological significance of this thyroid-pituitary interrelationship became more evident when Allen and Smith in 1916 and 1917 showed that removal of the hypophysis in tadpoles, among other effects, caused an involution of the thyroid with reduction in its size. Smith later adapted the pharyngeal route (previously used in dogs by Aschner and others)

to the rat and obtained similar results. He also demonstrated that implants or injections of extracts of anterior pituitary restored such involuted thyroids to normal or even caused hypertrophy, and established the existence of a specific hormonal factor now known as the thyrotropic hormone. So far this hormonal factor has not been entirely separated from the other hormones of the anterior pituitary and it is, therefore, not possible to say whether other pituitary factors will or will not stimulate the thyroid. Hisaw and others obtained a purified luteinizing fraction that caused thyroid hypertrophy. A thyroid stimulating substance has been found in the blood of thyroidectomized animals and in cases of Gull's disease but not in cases of Graves' disease. Eitel, Krebs and Loeser have shown that anterior pituitary extracts will cause hypertrophy of surviving thyroid cells in vitro. Marked hyperplasia of the thyroid beginning within a few hours occurs in susceptible animals. This hyperplasia is associated with a rapid loss of iodine from the thyroid, a corresponding increase in the blood iodine, an increase in the metabolic rate and in calcium and creatine excretion. The administration of iodine has an inhibitory effect on thyroid hyperplasia and also greatly reduces the high metabolic rate caused by pituitary extracts. (Iodine does not lower the increased metabolic rate produced by thyroxine.) Exophthalmos may develop as a late phenomenon in susceptible species (fish, birds, guinea pigs). It was quickly pointed out that this transient symptom complex was strikingly similar to that seen in Graves' disease. Unfortunately it has not helped in the elucidation of this symptom complex but it has further confirmed the fact that Graves' disease is a very complex polyglandular disturbance.

Growth is so constantly depressed by thyroidectomy alone and by hypophysectomy alone that the impression was formed that a thyroid component was necessary for the effectiveness of the growth hormone. In 1925 Evans reported that he had obtained growth in thyroidless rats and recently (1939) further reports that good growth may be obtained in thyroidectomized rats. However, he finds slightly better growth in animals with intact thyroids.

Thyroid-Gonad

This interrelationship was known to the ancients as evidenced by enlargement of the thyroid gland during puberty, menstruation, pregnancy and the menopause. Thyroxine is stated not to reduce the comb-

growth promoting effects of androgens but it certainly lessens the exophthalmos-promoting effects of testosterone propionate. There is abundant evidence that thyroxine reduces the action of estrogens. Abelin has shown that thyroxine will suppress estrus in the rat and Smelzer and others have shown that it reduces the size of the testis in doses too small to affect body weight and growth. It requires more estrone to induce estrus in rats that are given thyroxine. Estrone has been shown to depress the thyroid, as evidenced by involution, and increases the iodine store, while androgens do not have this effect. Indeed, there is evidence that they stimulate the thyroid.

Fluhman found that thyroxine decreased the activity of the gonadotropic factor. Removal of the ovaries causes a temporary enlargement of the thyroid (first noted in dogs) and Loeser has studied this reaction extensively in the guinea pig. He thinks it is mediated by way of the pituitary gland. It is well known that gonadectomy in animals usually leads to a depression and involution of the thyroid after the initial stimulation. This is also indicated in the slight lowering of the metabolic rate in castrates. Schockaert first showed that pituitary extracts caused a much more marked gonadotropic effect in thyroidectomized animals and we have repeatedly pointed out that in puberal rabbits goiter or subtotal thyroidectomy usually hastens sexual differentiation and greatly increases sexual activity. It is usual to see in such rabbits sexual activity at three months, while our two strains usually do not become sexually active until three and one-half to four and one-half months. Hill has made the important observation that ovaries transplanted to the ears of castrated male mice will maintain the prostate gland but if thyroxine is administered the prostate regresses to the castrate type. Also Tyndall and Lewin found that the increased sensitivity of hypophysectomized rats to menopause urine extract can be decreased by thyroxine administration. Thus they demonstrated a direct thyroid-gonad effect in addition to those (estrone) believed to be mediated through the pituitary. All of this experimental work appears to have a direct bearing on the age-old observations mentioned above. Thus the menstrual thyroid enlargement occurs at a time when the estrogens are at their lowest level and the androgens are relatively at their highest level. The thyroid enlargements occurring at the menopause, natural and surgical, and occasionally associated with the development of Graves' disease may also be connected with a decrease in estrogens. Myxedema also develops at the menopause and in contrast

with Graves' disease may be associated with a decrease in both estrogens and androgens.

Thyroid-Adrenal Cortex

There is a great deal of evidence for a thyroid-adrenal cortex interrelation. R. G. Hoskins (1910) reported that feeding large doses of thyroid to young guinea pigs caused hypertrophy of the adrenal cortex. Similar reports for cats and rats were made in 1916 (Hering and E. R. Hoskins). Cameron and Carmichel (1920), using rats, and many other observers have confirmed the above observations. In 1920 my colleagues and myself reported that sufficient but sublethal injury of the adrenals in rabbits by freezing or removal, with intact thyroids resulted in increase in O_2 consumption and CO_2 output in about 80 per cent of the animals used. This increase in metabolism began between the third and sixth days and lasted from a few days to several months. On the other hand, if the thyroid gland had been removed and the metabolic rate allowed to fall to the myxedema level prior to adrenal injury, this increase in heat production did not occur. Davis and Hastings have made similar observations on mice. The observation of Butcher that adrenalectomy hastens hair growth over shaved areas of white rats and that it takes larger amounts of thyroxine to hasten hair growth in normal rats than in adrenalectomized rats further suggests an antagonistic effect of the adrenal cortex on the action of thyroxine.

Adrenalectomized animals are very sensitive to thyroxine and several observers (Cameron, Koelsche) found that cortin offers some protection. Marine, Baumann and Cipra (1925) showed that feeding large quantities of a glycerol emulsion of fresh ox adrenal cortex significantly lowered the heat production in eight of eleven rabbits. Oehme (1936) reported that a cortical extract (cortidyn) partially protected guinea pigs against the action of thyroxine and inhibited the increased metabolism caused by 40 to 100 units of thyrotropic hormone, but did not inhibit thyroid hypertrophy.

Reiss and Peter have obtained a lowering of the blood iodine and involution of the thyroid with the cortical hormone. In cases of Graves' disease we have seen definite beneficial effects from cortical extracts. Richardson also reports a slight decrease in metabolic rate following cortical hormone administration. Other evidence supports the existence of a thyroid-cortical hormone interrelation. Thus many observers have

noticed failure to obtain striking hypertrophy of the adrenal cortex with anterior pituitary extracts in thyroidectomized rats and guinea pigs. Some observers have denied that the thyroid is necessary but a recent series of experiments in guinea pigs by Rosen and myself strikingly illustrate the importance of the thyroid for this hypertrophy. Loeser also showed that hypertrophy of the adrenal cortex occurred in thyroidectomized animals if given thyroxine with the anterior pituitary extract. This can be correlated with the occurrence of cortical hypertrophy following thyroxine alone if the pituitary gland is intact. Reiss and Peter have recently reported that cortical hormone lowered the blood iodine and involuted the thyroid.

Another type of evidence is the presence of a Graves' disease-like hyperplasia of the thyroid in those cases of Addison's disease associated with atrophy of the adrenal cortex. Chiari has reported two cases and I have observed one such case. Bastenie and Maes have obtained slight hypertrophy of the thyroid during the first few days following removal of the second adrenal somewhat comparable to the slight thyroid hypertrophy which follows ovariectomy and which is believed to be mediated by way of the pituitary.

The observation of Zwemer that thyroidectomy prolonged the lives of adrenalectomized cats and that feeding thyroid shortened their lives appears logical, although Weyman, using rats, could not confirm it.

To sum up then, there is much evidence from many angles that the adrenal cortex has an antithyroid action and it seems to be beyond question that these two organs have antagonistic effects. From the practical point of view it also appears certain that the total picture of Graves' disease with its creatinuria, loss of hair, muscular weakness, achlorhydria, pigmentation and persistent thymus involves, among other things, an adrenal insufficiency.

Thyroid-Chromaffin System

Some interrelation is indicated because thyroxine and epinephrine are derivatives of tyrosine, and because both of these hormones are powerful activators of metabolism through different mechanisms. Goldberg and others have shown in thyroidectomized lambs, and we have confirmed it in thyroidectomized rabbits, that the adrenal medulla is definitely hypertrophic. Barker and others showed that in rats thyroidectomy decreased and thyroid feeding increased the response to adrenalin. Seeley and

Cutler studying patients with myxedema (spontaneous and postthyroidectomy) found them to be less sensitive to adrenalin than normal individuals. Hering has shown that thyroid feeding increases the epinephrine store in the adrenal. Asher and Flack first showed that the blood pressure response in rabbits to a given dose of adrenalin was greater after stimulation of the thyroid nerve with intact thyroid than before. This has been confirmed particularly by Cannon and his co-workers. Oswald has shown that a similar increase in the blood pressure response to adrenalin may be obtained by the intravenous injection of iodothyroglobulin and the effect produced is proportional to the iodine content of the thyroglobulin injected. The Goetsch epinephrine test for exophthalmic goiter may be a clinical application of increased sensitivity to adrenalin. All these observations would support the original view of Asher and Flack that the thyroid hormone increases the irritability of the sympathetic nervous system and sensitizes the tissues innervated by it so that they are more susceptible to stimulation by epinephrine.

Thyroid-Thymus

In 1912 Gudernatsch observed that thymus gland fed to tadpoles increased the rate of growth, definitely retarded metamorphosis and offered some protection against the effects of thyroid feeding. These observations have been abundantly confirmed. Hoskins found that thyroid fed to guinea pigs caused the thymus to enlarge. This observation has been confirmed and extended to other species. Thus Kahn and Spiegle found that thyroid feeding caused a rapid proliferation of the thymus cells in frogs. Albertini claims to have produced a condition resembling status thymolymphaticus by thyroid feeding. Thyroidectomy has regularly been found to hasten involution of the thymus. Removal of the pituitary gland in dogs, according to Houssay, causes involution of the thymus. Roelandt and others found that immature rabbits (as is true of immature animals generally) are less sensitive to thyroxine than adults but that thymectomy increases their sensitivity. They also found that a thymus extract made adult rabbits less sensitive to thyroxine. Asher and his co-workers have prepared a peptide extract of calf's thymus which they call thymocresin. This extract promoted growth and was rich in the sulphhydryl groups. Nowinski obtained some protection against thyroxine action by the use of thymocresin.

In diseases in which thyroid activity is believed to be increased, as

in Graves' disease and acromegaly, thymus hypertrophy frequently occurs. All these effects indicate some kind of antagonism between the thyroid and thymus glands. In prepuberal animals the condition of the adrenal cortex appears to be the most powerful factor in determining the status of the thymus. Hence in conditions with excessive thyroid activity or decreased adrenal cortex activity thymectomy would not appear to be a rational therapeutic measure, and I believe thymectomy is no longer done in the treatment of Graves' disease.

Thyroid-Parathyroid

The view that the parathyroid glands could function vicariously for the thyroid was disproved by Gley's demonstration in the rabbit that the so-called acute effects of thyroidectomy seen in dogs and cats were due to the accompanying parathyroidectomy. The strikingly different symptoms following thyroidectomy and parathyroidectomy appear to have established independent functions for these glands, but during the past decade evidence has accumulated indicating that they are at least complementary in certain of their functions. The work on experimental rickets and especially the work of Aub and his co-workers on exophthalmic goiter, thyroid feeding and myxedema shows that the thyroid is also concerned in the metabolism of calcium and phosphorus. The idea that excessive calcium ingestion was a causal factor in endemic goiter was suggested a century ago (McClellan, 1837). Aub has shown that in Graves' disease the calcium excretion is greatly increased while in myxedema it is decreased. Both thyroid feeding and the administration of the thyrotropic hormone greatly increase calcium excretion. Excessive thyroid feeding causes parathyroid hypertrophy. Thyroidectomy in rabbits on diets with normal calcium phosphorus ratios usually causes involution of the parathyroids. The increased thyroid activity in animals (dogs, rats, rabbits) on the rachitogenic diets is associated with parathyroid hypertrophy. It may, therefore, be significant that no parathyroid changes have been demonstrated in Graves' disease.

Thyroid-Creatine

Graves' disease is usually associated with creatinuria and Denis first demonstrated that the muscle creatine was markedly reduced. Feeding thyroid to animals reduces the muscle creatine about 20 per cent and the heart muscle creatine about 40 per cent. In myxedema there is ordinarily

no creatinuria but if such cases are fed desiccated thyroid, Richardson and Shorr have shown that creatinuria may appear before any detectable rise in the metabolic rate occurs, and that the creatinuria may stop when the metabolic rate is restored to normal, although the patient continues to take desiccated thyroid. Carson and Palmer had previously noted that the creatinuria produced by thyroid feeding in normal subjects often stopped even though the metabolic rate was rising. The thyrotropic hormone also causes creatinuria in animals with intact thyroids. Creatine tolerance is lowered to about 40 per cent in cases of Graves' disease and iodine therapy raises this tolerance to 65 to 70 per cent. Dinitrophenol also causes a sharp increase in creatinuria (Pugsley). Adrenalectomy causes a marked drop in muscle creatine associated with creatinuria, and Maranon has shown that cortical hormone administration decreases the creatinuria of Addison's disease. This suggests that possibly the adrenal cortex hypertrophy which follows thyroid feeding is a protective mechanism which aids in the resynthesis of phosphogen.

Thyroid-Vitamins

A considerable but conflicting literature has accumulated on the relation of the various vitamins to thyroid function.

Vitamin A. Many observers have noted some protective action of vitamin A in experimental hyperthyroidization (Abelin and H. Euler). Abelin showed that thyroxine reduced the vitamin A content of the liver and Wegelin's recent work indicates that vitamin A offers some protection to the stores of liver glycogen following thyroxine administration. Vitamin A also appears to have a slight inhibiting effect on the thyrotropic hormone but does not change the blood iodine levels (Elmer).

Vitamins B_1 and B_2. Conflicting results are reported. B_1 in large doses appears to protect animals against the weight loss due to thyroxine administration (Sure) and thyroxine hastens the development of beriberi in fowls. B_1 does not inhibit the action of the thyrotropic hormone (Elmer). Dr. Sandberg in our laboratory was unable to involute hyperplastic thyroids of rabbits with large amounts of the B complex.

Vitamin C. Vitamin C appears to have a more marked effect on the thyroid than either vitamin A or B. Many observers (Mouriquand and Michel, 1920, and Nobel and Wagner, 1923) have shown that thyroxine administration hastens the development of scurvy. It is well known that hypertrophy of the thyroid occurs during the developmental stages of

scurvy, associated with an increase in the metabolic rate and an increase in the blood iodine (Fasold). Thyroid feeding depletes the stores of vitamin C, while thyroidectomy increases them. The excretion of ascorbic acid has been found to be lowered in Graves' disease and to be increased after partial thyroidectomy (Lewis). Ascorbic acid appears to decrease the action of thyrotropic hormone on the thyroid gland (Marine et al, Elmer et al). Plehwe has been able to reduce the creatinuria of Graves' disease with large doses of ascorbic acid, but no appreciable beneficial effects on Graves' disease have been reported from the use of ascorbic acid.

Vitamin D. The quite frequent occurrence of thyroid enlargement in human and experimental rickets led to the suggestion of a thyroid-vitamin D relationship, but the work of Thompson has shown that in the white rat experimental goiter and experimental rickets could be dissociated, that is, she could obtain goiter and rickets or prevent rickets and obtain goiter, or produce rickets without goiter by giving or withholding iodine and viosterol. The long clinical association of endemic goiter and high calcium intakes; the increased calcium excretion following thyroid feeding and the frequent association of goiter and rickets has kept up a lively interest in the relation of the thyroid gland to rickets.

Nitsche thought that the low metabolic rate and the thyroid enlargement of rickets was indicative of a thyroid deficiency. The observation of Kunde and Williams that cod liver oil would not cure rickets in thyroidectomized rats suggests that possibly the thyroid may be important in the utilization of vitamin D. In the rabbit we have not observed that ergosterol influenced the development of goiter.

In summary, one can discern a similarity of the effects for all four of the vitamins mentioned, that is, hyperthyroidization increases the needs for, and tends to deplete the stores of these vitamins. Hence it is logical to expect that hypervitaminosis would offer some protection against thyroxine administration. In the early stages of B_1 and C avitaminosis there is increased metabolism, increased blood iodine and moderate thyroid hypertrophy followed by decrease as the avitaminosis progresses. The evidence, taken as a whole, indicates that vitamins do not specifically affect the thyroid and, as Means has pointed out, there is no evidence that the administration of vitamins appreciably benefits either Graves' disease or Gull's disease.

LIBRARY NOTES

RECENT ACCESSIONS

"Possession does not imply approval"

Abderhalden, E. *Die Grundlagen unserer Ernährung.* 4. Aufl.
Berlin, Springer, 1939, 193 p.

American Medical Association. Bureau of Medical Economics. *Organized payments for medical services.*
Chic., Amer. Med. Assoc., 1939, 185 p.

Barborka, C. J. *Treatment by diet.* 4. ed.
Phil., Lippincott, [1939], 691 p.

Beck, A. C. *Obstetrical practice.* 2. ed.
Balt., Williams, 1939, 858 p.

Berry, R. J. A. *Your brain and its story.*
London, Oxford Univ. Press, 1939, 165 p.

Bing, R. *Textbook of nervous diseases.* Translated. . .by W. Haymaker from the 5. German ed.
St. Louis, Mosby, 1939, 838 p.

Borst, M. *Pathologische Histologie.* 3 Aufl.
Berlin, Springer, 1938, 522 p.

Brickel, A. C. J. *Surgical treatment of hand and forearm infections.*
St. Louis, Mosby, 1939, 300 p.

Brochère, F. *Odonto-stomatologie; les problèmes de la pratique quotidienne.*
[Etampes, Soc. Régionale d'Imprim. et de Pub., 1938], 485 p.

Burdon, K. L. *Medical microbiology.*
N. Y., Macmillan, 1939, 763 p.

Campbell, W. C. *Operative orthopedics.*
St. Louis, Mosby, 1939, 1154 p.

Carrière, G. L.; Huriez, C. & Codron, M. *Adénopathies généralisées de l'adulte.*
Paris, Doin, 1939, 119 p.

Carter, C. F. *Microbiology and pathology.* 2. ed.
St. Louis, Mosby, 1939, 755 p.

Caullery, M. *Les progrès récents de l'embryologie expérimentale.*
Paris, Flammarion, [1939], 236 p.

Clark, W. E. Le G. *The tissues of the body.*
Oxford, Clarendon Press, 1939, 372 p.

Clavel, C. & Latarjet, M. *Anatomie chirurgicale du crâne et de l'encéphale.*
Paris, Doin, 1938, 258 p.

Collens, W. S. & Wilensky, N. D. *Peripheral vascular diseases.*
Springfield, Ill., Thomas, [1939], 243 p.

Congresso (4) Internazionale di Patologia Comparata, Rome, 1939. [*Reports*].
[Milano, Stucchi, 1939], v. 1.

Crampton, C. W. G. *Training for championship athletics.*
N. Y., Whittlesey, [1939], 303 p.

Cutler, E. C. & Zollinger, R. M. *Atlas of surgical operations.*
N. Y., Macmillan, 1939, 181 p.

Dogliotti, A. M. *Anesthesia: narcosis, local, regional, spinal.*
Chic., Debour, 1939, 680 p.

Dutton, W. F. *Headache and head pains.*
Phil., Davis, 1939, 301 p.

Ewalt, J. R.; Parsons, E. H.; Warren, S. L. [et al.] *Fever therapy technique.*
N. Y., Hoeber, [1939], 161 p.

Ey, H. & Rouart, J. *Essai d'application des principes de Jackson à une conception dynamique de la neuro-psychiatrie.*
Paris, Doin, 1938, 114 p.

Fellinger, K. *Die Fettleibigkeit.*
Berlin, Urban, 1939, 222 p.

Filderman, J. *Technique des coiffes métalliques et des coiffes avec mortaises.*
Paris, Information Dentaire, 1938, 135 p.

Fisher, A. G. T. *Treatment by manipulation.* 3. ed.
N. Y., Hoeber, 1939, 255 p.

Geipel, P. *Über Schwefelsäurevergiftung. Der Fall Zäuner.*
[Dresden, Gutzmann, 1938], 132 p.

Greenhill, J. P. *Office gynecology.*
Chic., Year Book Publishers, [1939], 406 p.

Hallermann, W. *Der plötzliche Herztod bei Kranzgefässerkrankungen.*
Stuttgart, Enke, 1939, 215 p.

Hauser, E. D. W. *Diseases of the foot.*
Phil., Saunders, 1939, 472 p.

Heupke, W. *Die Faeces des Menschen.*
Dresden, Steinkopff, 1939, 115 p.

Hill, F. E. *Educating for health; a study of programs for adults.*
N. Y., American Assoc. for Adult Educ., 1939, 224 p.

Hittmair, A. *Blutdiagnostik für den praktischen Arzt.* 2. Aufl.
Berlin, Urban, 1939, 115 p.

Hovelacque, A. & Turchini, J. *Anatomie et histologie de l'appareil urinaire et de l'appareil génital de l'homme.*
Paris, Doin, 1938, 306 p.

Huddleson, I. F. *Brucellosis in man and animals.*
N. Y., Commonwealth Fund, 1939, 339 p.

Jackson, D. E. *Experimental pharmacology and materia medica.* 2. ed.
St. Louis, Mosby, 1939, 906 p.

Ker, C. B. *Manual of fevers.* 4. ed.
London, Milford, 1939, 354 p.

Kleitman, N. *Sleep and wakefulness as alternating phases in the cycle of existence.*
Chic., Univ. of Chic. Press, [1939], 638 p.

Köhler, L. *Das Aufstellen einer ganzen Prothese und ihre Fertigstellung.*
Berlin, Berlinische Verlagsanstalt, 1939, 129 p.

Kosch, A. *Handbuch der deutschen Arzneipflanzen.*
Berlin, Springer, 1939, 444 p.

Kudo, R. R. *Protozoology.*
Springfield, Ill., Thomas, [1939], 689 p.

Lebourg, L. *Les dystrophies dentaires de la syphilis héréditaire.*
Paris, Doin, 1939, 159 p.

LeComte, R. M. *Manual of urology.* 2. ed.
Balt., Williams, 1939, 295 p.

Lemay, P. *Cancer et tréphones de Carrel.*
Paris, Le François, 1938, 132 p.

McCurdy, J. H. & Larson, L. A. *The physiology of exercise.* 3. ed.
Phil., Lea, 1939, 349 p.

McLester, J. S. *Nutrition and diet in health and disease.* 3. ed.
Phil., Saunders, 1939, 838 p.

Macquet, P. A. A. *Les calculs de l'uretère.*
Paris, Masson, 1939, 186 p.

Martius, H. E. F. *Gynecologic operations and their topographic-anatomic fundamentals.*
Chic., Debour, 1939, 486 p.

May, P. *The chemistry of synthetic drugs.* 4. ed.
London, Longmans, [1939], 370 p.

Mills, C. A. *Medical climatology.*
Springfield, Ill., Thomas, [1939], 296 p.

Morenas, L. *Entérites et colites parasitaires.*
Paris, Masson, 1939, 168 p.

Nielsen, H. *Forelaesninger over klinisk endokrinologi.*
København, Levin, 1938, 2 v. in 1.

Ochsner, E. W. A. & Mahorner, H. R. *Varicose veins.*
St. Louis, Mosby, 1939, 147 p.

Payne, E. A. *Harry Wyatt of Shansi, 1895-1938.*
London, Carey, [1939], 128 p.

Pedersen-Bjergaard, K. *Comparative studies concerning the strengths of oestrogenic substances.*
Copenhagen, Munksgaard, 1939, 198 p.

Plimmer, R. H. A. & Plimmer, (Mrs.) V. G. (Sheffield). *Food, health, vitamins.* 8. ed.
London, Longmans, [1938], 233 p.

Ross, J. M. *Post-mortem appearances.* 4. ed.
London, Milford, [1939], 275 p.

Roufogalis, S. *Lungenabszess und Lungenabszedierungen im Kindesalter.*
Leipzig, Barth, 1939, 166 p.

Scherber, G. *Die Bekämpfung der Geschlechtskrankheiten und der Prostitution.* 2. Aufl.
Wien, Maudrich, 1939, 207 p.

Schick, F. *Der Mund als Spiegel der Krankheit.*
Leipzig, Barth, 1939, 158 p.

Schmidt, H. J. *Zahnärztliche Statistik.*
Stuttgart, Marquardt, 1938, 106 p.

Simon, R. *Les traitements orthopédiques et chirurgicaux des rhumatismes chroniques.*
Paris, Doin, 1938, 168 p.

Smith, F. C. *Proctology for the general practitioner.*
Phil., Davis, 1939, 386 p.

Sutton, R. L. & Sutton, R. L., Jr. *Diseases of the skin.* 10. ed.
St. Louis, Mosby, 1939, 1549 p.

Thewlis, M. W. *Preclinical medicine.*
Balt., Williams, 1939, 223 p.

Vaughan, W. T. *Primer of allergy*
St. Louis, Mosby, 1939, 140 p.

Villey-Desmeserets, G. *La psychiatrie et les sciences de l'homme.* Paris, Alcan, 1938, 194 p.

Voronoff, S. *Greffe des glandes endocrines.* Paris, Doin, 1939, 286 p.

Wegner, R. N. *Das Anatomenbildnis.* Basel, Schwabe, [1939], 199 p.

Weissenbach, R. E. J. & Françon, F. *Les rhumatismes, maladies sociales.* Paris, Doin, 1939, 206 p.

PROCEEDINGS OF ACADEMY MEETINGS

STATED MEETINGS

October 5—*The New York Academy of Medicine.* Executive Session—a] Reading of minutes. ¶ Papers of the evening—The treatment of pyogenic infections with special reference to chemotherapy—a] Introductory—general observations on bacteremia, Emanuel Libman, Consulting Physician, The Mount Sinai Hospital; b] Osteomyelitis, D. B. Phemister, Professor of Surgery, University of Chicago; c] Otitis media and its extensions, Edmund P. Fowler, Jr., Assistant Clinical Professor of Otolaryngology, College of Physicians and Surgeons. ¶ Report on election of members.

October 19—*The Harvey Society (in affiliation with The New York Academy of Medicine)* The First Harvey Lecture, "Electrophoretic Analysis and the Constitution of Native Fluids," Arne Tiselius, Professor of Biochemistry, Fysikalisk-Kemiska Institutionen, Uppsala Universitet, Sweden.

November 2—*The New York Academy of Medicine.* Executive Session—a] Reading of the Minutes; b] Report of Nominating Committee. ¶ Papers of the Evening (Graduate Fortnight) a] Physiology of the ovaries, Philip E. Smith, Professor of Anatomy, Columbia University; b] Physiology of testes and therapeutic application of male sex hormones, Carl R. Moore, Professor of Zoology, University of Chicago. ¶ Report on Election of Members.

November 16—*The Harvey Society (in affiliation with The New York Academy of Medicine).* The Second Harvey Lecture, The Biological Significance of Nicotinic Acid, C. A. Elvehjem, Professor of Biochemistry, College of Agriculture, University of Wisconsin.

SECTION MEETINGS

October 3—*Section of Dermatology and Syphilology.* Presentation of cases—a] Clinics; b] Hospitals; c] Members. ¶ General Discussion. ¶ Executive session.

October 6—*Section of Surgery.* Reading of the minutes. ¶ Presentation of cases—Rectus transplantation for midline incisional hernia, John E. Sutton, Jr.; Discussion, Seward Erdman. ¶ Papers of the evening—a] End results of silk repair in 1000 hernia operations, Roland L. Maier, William Ross McCarty (by invitation); Discussion, Fenwick Beekman; b] A clinical study of the use of alloy steel wire in hernia repair, Louis René Kaufman; Discussion, Paul Kurt Sauer; c] The injection treatment of hernia, clinical-pathological evidence for its rationale, Carl O. Rice, University of Minnesota (by invitation); Discussion, David H. M. Gillespie. ¶ General discussion. ¶ Executive session.

October 10—*Section of Neurology and Psychiatry.* Reading of the minutes. ¶ Papers of the evening—a] The diagnosis of

arachnoiditis and varicosities of the spinal cord and cauda equina by direct visualization of the nerve roots with a myeloscope, J. Lawrence Pool (by invitation); Discussion, Byron Stookey, Charles A. McKendree, Ira Cohen, Richard Brickner, E. L. Stern; b] Studies on headache—pain sensitive structures in the cranium and their significance, B. S. Ray, H. G. Wolf; Discussion, Joseph C. Hinsey, Ph.D. (by invitation), Byron Stookey, H. A. Riley, L. Hausman, Tracy Putnam; c] Injuries to the deep and superficial peroneal nerves complicating ankle sprain, George H. Hyslop; Discussion, Lewis C. Wagner, Samuel Brock, Byron Stookey.

October 12—*Section of Pediatrics.* Reading of the minutes. ¶ Papers of the evening—a] The clinical picture of tuberculosis, Edith Lincoln; b] The tuberculin test in relation to case-finding—especially from the general practitioner's viewpoint, Herman Schwarz; c] The roentgenographic diagnosis of tuberculosis in infants and young children, John Caffey. ¶ Discussion, Charles Hendee Smith, Bela Schick, Herbert R. Edwards, William H. Meyer, Camille Kereszturi. ¶ Executive session.

October 16—*Section of Ophthalmology.* Instruction hour 7:00 to 8:00. Further principles in plastic surgery of the eye, Wendell L. Hughes. Demonstration 8:00 to 8:30. Sections and photomicrographs showing comparative histology of the eye, Mr. Roy M. Allen (by invitation). ¶ Reading of the minutes. ¶ Presentation of cases—a] Sarcoid of the lacrymal gland, David Wexler; b] Streptothrix infection of the lower cannaliculus, with calculus formation, David O. Shepard (by invitation). ¶ Paper of the evening, Chorioretinal arteriolar necrosis in a case of malignant hypertension, Martin Cohen. ¶ General discussion. ¶ Executive session.

October 17—*Section of Medicine.* Reading of the minutes. ¶ Papers of the evening—a] Ultrafiltrable magnesium studies in hyperthyroidism, Louis J. Soffer; Discussion, George Baehr; b] The use of deproteinated pancreatic extract (depropanex) in the treatment of intermittent claudication, Irving Sherwood Wright. ¶ General discussion. ¶ Executive session.

October 18—*Section of Genito-Urinary Surgery.* Reading of the minutes. ¶ Papers of the evening—a] Hypertension—the problem, the study, the future, Stanford W. Mulholland, Temple University, Philadelphia (by invitation); b] The surgical treatment of hypertension in unilateral kidney disease, Reed Nesbit, University of Michigan, Ann Arbor (by invitation). ¶ General discussion. ¶ Executive session.

October 18—*Section of Otolaryngology.* Reading of the minutes. ¶ Papers of the evening—a] Surgery of the auricle including total reconstruction and flop ears, Gerald H. Cox (by invitation); b] Nasal plastic surgery, Clarence R. Straatsma (by invitation); c] Oral plastic surgery, Henry S. Dunning; Discussion, Jerome P. Webster, William H. Holden, Douglas B. Parker (by invitation). ¶ General discussion.

October 20—*Section of Orthopedic Surgery.* Reading of the minutes. ¶ Presentation of cases—a] Toes and tarsal amputations, Halford Hallock; b] Mid-tarsal amputation, Frederick Thompson (by invitation; c] Simms amputation, John C. McCauley; d] Lower tibial amputation, Beverly C. Smith; e] Upper tibial amputation with fibular head en situ, Joseph B. L'Episcopo; f] Upper tibial amputation with fibula removed, Mather Cleveland; g] Gritti-Stokes amputation, Edward Winant (by invitation); h] Mid-thigh amputation, Ernest Meyers (by invitation); i] Hip joint disarticulation, Leo Mayer. ¶ Paper of the evening, Cineplastic amputations, Henry Kessler, Newark (by invitation); Discussion, Henry H. M. Lyle. ¶ General discussion. ¶ Executive session.

Section of Obstetrics and Gynecology. Because of conflict in dates with the Graduate Fortnight, the meeting of the Section was not held.

Dermatology and Syphilology. The regular meeting of the Section was not held because of the date falling on Election Day and also due to the meeting of the American Academy of Dermatology and Syphilology in Philadelphia on November 6, 7, and 8.

Surgery. The Section of Surgery consented to forego its November meeting because of conflict in dates with the Graduate Fortnight.

NOVEMBER 8—*Historical and Cultural Medicine.* Reading of the minutes. ¶ Papers of the evening—Symposium on Syphilis—a] Introduction, John L. Rice; b] Contributors to the knowledge of syphilis since 1492 (illustrated with lantern slides), Herman Goodman; c] Old epidemics of syphilis, Theodore Rosenthal. ¶ Discussion—C. C. Pierce (by invitation), Leona Baumgartner (by invitation), Harry H. Sobotka, Richard C. Holcombe, Upper Darby, Pa. (by invitation). ¶ General discussion.

NOVEMBER 9—*Pediatrics.* Reading of the minutes. ¶ Papers of the evening—a] Long Island Medical College—An eight-year-old boy with generalized decalcification possibly hyperparathyroidism with metabolic studies, H. C. Eisenberg (by invitation), Louis E. Weymuller (by invitation); b] Cornell University Medical College—Pyrexia associated with abdominal pain of six months' duration in a thirteen-year-old boy, James M. Hanks (by invitation), Samuel Z. Levine); c] New York Post-Graduate Medical School—Report of a case with clinical manifestations of a blood dyscrasia, Irving Posner (by invitation); d] Mount Sinai Hospital—Fulminating meningococcemia with bilateral adrenal hemorrhage (Waterhouse Friderichsen syndrome), J. A. Danciger (by invitation), Bela Schick; e] Lincoln Hospital—Johnson's disease (erythema multiforme bullosum), Harry Ageloff (by invitation). ¶ General discussion. ¶ Executive session.

NOVEMBER 14—*Combined meeting of Neurology and Psychiatry with the New York Neurological Society.* Papers of the evening—a] Spastic pseudosclerosis: Cases with familial and non-familial incidence, Charles Davison, A. M. Rabiner; Discussion by M. Keschner, I. S. Wechsler; b] On epilepsy, Otto Marburg (by invitation); c] Pathogenesis of syphilitic blindness and the restoration of vision by surgery, Louis Hausman; Discussion by Bernard Sachs, Foster Kennedy. ¶ Executive session.

NOVEMBER 15—*Otolaryngology.* Reading of the minutes. ¶ Papers of the evening—a] Some late results of brain abscess; Presentation of patients, Ira Cohen, Abraham Kaplan (by invitation); b] Management of brain abscess of otorhinogenic origin, Joseph E. J. King. ¶ Discussion by Foster Kennedy, Isidore Friesner, Robert E. Buckley, Lewis D. Stevenson, Edgar A. Kahn, Ann Arbor (by invitation). ¶ General discussion. ¶ Executive session.

Genito-Urinary Surgery. On account of the November meeting of the New York Society of the American Urological Association, the Section decided to forego their meeting this month.

NOVEMBER 17—*Orthopedic Surgery.* Reading of the minutes. ¶ Papers of the afternoon — a] Charcot neuroarthropathy, Maurice M. Pomeranz, Abraham S. Rothberg (by invitation); b] End-result study of posterior bone-block operations at the ankle, Lewis Clark Wagner; c] Osteochondritis dissecans of the knee, Walker Swift; d] Muscle metabolism as an etiological factor in scoliosis, John Cobb (by invitation); e] Treatment of osteogenic sarcoma, Albert Ferguson (by invitation); f] Sclerosing osteomyelitis of the neck of the femur, Nicholas Ransohoff; g] Aspects of the surgical treatment of tuberculosis of the spine in children, William H. vonLackum (by invitation); h] An operation for flat feet, Isadore Zadek; i] Further

experiences with celloidin tube implantations for tendon injuries, Leo Mayer; j] Congenital club feet, J. Neill Garber (by invitation); k] Rare congenital deformity of the right upper extremity, consisting of double arms, three hands and sixteen fingers, Harry C. Stein (by invitation). ¶ General discussion. ¶ Executive session.

NOVEMBER 20 — *Ophthalmology.* Instruction hour 7:30 to 8:30—Slit-lamp microscopy of the vitreous, Milton Berliner. ¶ Reading of the minutes. ¶ Presentation of cases—a] Groenouw's corneal dystrophy, Walter Hipp; b] Lymphangioma of the orbit, Herman Goldberg (by invitation); c] Congenital retinal folds, Frederick Theodore (by invitation). ¶ Papers of the evening — a] The relationship of drusen of the optic nerve to tuberous sclerosis, Algernon Reese; Discussion by Ferdinand Koch (by invitation); b] Treatment of syphilitic optic atrophy due to chiasmal arachnoiditis, Louis Hausman; Discussion by Bernard Sachs, Thomas Johnson. ¶ Executive session.

NOVEMBER 21—*Medicine.* Reading of the minutes. ¶ Moving pictures — a] Pneumonia—Diagnosis and treatment, Norman Plummer, H. K. Ensworth (by invitation). ¶ Papers of the evening—a] Heparin and other inhibitors of blood coagulation, Erwin Chargaff (by invitation); b] Clinical experiences with heparin, Kenneth B. Olson (by invitation); Discussion by Allen O. Whipple, Paul Reznikoff. ¶ General discussion.

NOVEMBER 28 — *Obstetrics and Gynecology.* Reading of the minutes. ¶ Presentation of cases — a] Masculinizing tumors of the ovary—Lantern slides, Salo M. Boltuch (by invitation); Discussion by Leon Motyloff (by invitation), Howard E. Lindeman; b] Torsion of the non-pregnant, non-myomatous uterus, Locke L. Mackenzie, Anna Mimelman (by invitation). ¶ Papers of the evening—a] Ruptured uteri—Analysis of 59 cases with symptoms, diagnosis and pathology, Hugh C. McDowell, Buffalo (by invitation); b] Histopathology of uterine scar, Norman W. Elton, Buffalo (by invitation). ¶ Discussion opened by Lewis F. McLean (by invitation).

AFFILIATED SOCIETIES

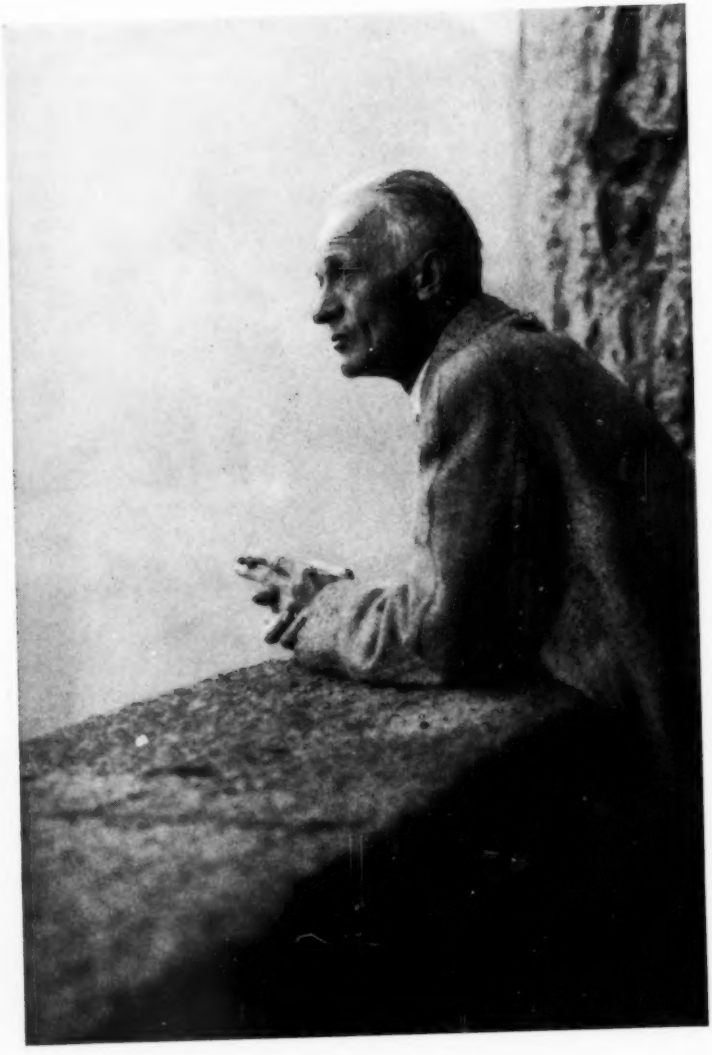
OCTOBER 16—*New York Roentgen Society (in affiliation with The New York Academy of Medicine).* Presentation of cases by members of the society. ¶ Executive session.

OCTOBER 18—*New York Section of the Society for Experimental Biology and Medicine.* The metabolism of human spermatozoa, John MacLeod (introduced by J. C. Hinsey). ¶ Identity of "inhibitor" and antibody in extracts of virus-induced rabbit papillomas, William F. Friedewald (introduced by Peyton Rous). ¶ The pathology of B_6 deficiency in the rat and the response to treatment with 2-methyl-3-hydroxy-4, 5-dihydroxymethylpyridine (Vitamin B_6), William Antopol, Klaus Unna (by invitation). ¶ The identity of the glycotropic (anti-insulin) substance of the anterior pituitary gland, Jerome Grattan (introduced by H. Jensen). ¶ The mechanism of pituitary gonadotropic antagonism, Sibylle Tolksdorf (introduced by H. Jensen). ¶ Acceleration of hemolysis in relation to chemical structure. II. The straight-chain alcohols, Eric Ponder, Chester Hyman (by invitation). ¶ Agglutination of endocarditis streptococci, Ward J. MacNeal, Martha Jane Spence (by invitation), Marie Wasseen (by invitation). ¶ The in-vitro production of glucuronic acid during phosphorus and chloroform poisoning, Ernest Bueding, Peter Ladewig (introduced by Isidor Greenwald).

New York Pathological Society. Because of conflict in dates with the Graduate Fortnight, this Society held no meeting in October.

NOVEMBER 20—*New York Roentgen Society (in affiliation with The New York Academy of Medicine).* Papers of the evening—a] Some studies on the effect of Roentgen rays on bone growth in rats—A preliminary report, Charles L. Hinkel (by invitation); b] Roentgen and histological studies of calcification in the spleen, Edwin F. Gray (by invitation); c] Anomalies of the cervical spine, Murray M. Friedman (by invitation); d] Megaesophagus, Robert P. Ball; e] Some experiences with cholangiography, Haig H. Kasabach. ¶ Discussion. ¶ Executive session.

NOVEMBER 30—*The New York Pathological Society (in affiliation with The New York Academy of Medicine).* Case report—Endocarditis with yeast infection of the blood stream, Silik H. Polayes, Cumberland Hospital. ¶ Papers of the evening—a] Renal hyperparathyroidism in childhood, Dorothy H. Andersen (by invitation), Babies Hospital; b] The architecture of the amyloid kidney, Jean R. Oliver, Long Island College Hospital.



HARVEY WILLIAMS CUSHING

1869 - 1939

IN MEMORIAM

HARVEY WILLIAMS CUSHING

Great Physician, Great Surgeon,
The Scholar in Medicine

The death of Harvey Cushing on October seventh of this year brought genuine sorrow to the entire medical world and to every member of The New York Academy of Medicine, of which he was an Honorary Fellow these many years.

Since the death of Sir Victor Horsley, Cushing was the unquestioned leader in brain surgery and was personally responsible for vast achievements recorded in that special line of surgical endeavor. It is fortunate for us that his fame as a teacher attracted pupils from all over the world, who will be able in the United States and in many countries of Europe, to continue the good work he inaugurated. If Cushing had been merely a great surgeon, it would be immodest on my part to attempt an estimate of his services and I am certain that some one, if not several of his distinguished pupils will give a very accurate estimate of his surgical skill. The great surgeon was an even greater clinician, who kept his special line of work and thought in intimate contact with general medicine and above all, with neurology and endocrinology.

The greater the specialist the more he feels his allegiance to medicine in general. Medical science profits by his special skill in research without implying that general medicine, in any way, controls or supplants the specialty. Cushing contributed much of great value to the ever troublesome question of brain localization, while his famous work on the pituitary proved to be of fundamental importance for neurology and endocrinology. Those of us who had occasion to see him at work at the Peter Bent Brigham Hospital realized his success was due to a keen intellect, a fine grasp of neurological problems and a most painstaking technique combined with the keenest sense of responsibility toward the fate of the patient. The patient's welfare was the prime consideration; no willingness on his part to sacrifice one inch more of brain substance than was absolutely necessary. He was indeed a great master, a marvelous teacher who set an example that every pupil would do well to follow. His pupils appreciated this and no master in medicine or surgery ever had a more devoted following. His devotion to his former teacher, Kocher, was demonstrated in most convincing fashion in 1931, in Berne, while he was attending the First International Neurological Congress.

Cushing's fellow neurologists recognized their indebtedness to him by electing him President of the American Neurological Association in 1923, four years before he was made President of the American Surgical Association. Similar honors may have meant little to him; they were showered upon him by universities here and abroad. Cambridge in England, The Royal College of Surgeons of England, the University of Toronto, of Edinburgh, the Universities of Paris, Strasbourg, Brussels, Berne paid honor to him; not to mention special degrees conferred on him by Jefferson, Dartmouth, Yale, Harvard, and Trinity College, Dublin.

In addition to the services rendered the profession, mention must be made of his distinguished work during the World War, when he was Director of the United States Base Hospital, Number Five, attached to the British Expeditionary Forces in France, and later on was appointed Senior Consultant in neurological surgery. The United States, Britain and France recognized the unusual brilliance of his work. Indefatigable worker as he was, he found time even during the years of the War to record his experiences, thoughts and well controlled emotions in a diary which was revealed later on in

"From a Surgeon's Journal" which made delightful reading when published in 1936.

The greatness of the man was revealed not only in surgical work, but in his sympathy for the untold suffering of the wounded. His talent as a writer and his broad human interests had been made known to the entire English speaking world in his two volume "Life of William Osler" for which he received the Pulitzer Prize in 1925. Osler and Cushing were indeed kindred spirits and intimate friends; both added, each in his way, to the high present-day rating of American medicine.

I cannot attempt to give a list of Cushing's many neurological and neurosurgical contributions. Of prime importance were "Tumors of the Acoustic Nerve" (with Doctor Bailey) in 1917; "A Classification of the Gliomata" in 1928; "Intracranial Tumors and the Pituitary Body and the Hypothalamus" in 1932. More important than all these publications are the records he left at the Peter Bent Brigham Hospital of the work done by him from 1912 to 1932, when he was retired because he had reached the age limit for surgical service.

From 1932 to 1937, he served his Alma Mater at New Haven as Sterling Professor of Neurology, thus evincing his close link to the mother specialty and resting on the laurels he had won in almost forty years of neurosurgical activity.

In spite of some physical disabilities he was mentally alert to the last, full of the joy of life and ever ready to help others with advice given in his own peculiar kindly spirit. Like Osler, Cushing was a real friend to hundreds. He himself has linked the two names. Let us continue to think of both of them as men who enriched medicine and proved that great men of science are true benefactors to all mankind.

BERNARD SACHS

DEATHS OF FELLOWS

BRIDGES, MILTON ARLANDEN: 850 Park Avenue, New York City; born in New York City, May 20, 1894; died in New York City, August 19, 1939; received the degree of B.S. from Columbia University in 1915 and graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1919; elected a Fellow of the Academy October 6, 1927.

Dr. Bridges was assistant clinical professor of medicine at the New York Post-Graduate Medical School, Columbia University; associate physician and chief of the Diagnostic Clinic at that institution; director of medicine to the Department of Correction Hospitals and secretary of its medical board; and consulting physician to the Sea View Hospital. He was a diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, a Fellow of the American Medical Association and a member of the State and County Medical Societies. Dr. Bridges wrote "Dietetics for the Clinician" and "Analyses of Foods and Beverages" and lectured on various aspects of metabolism.

CASSELL, JAMES WILSON: 30 East 40 Street, New York City; born in Lexington, Kentucky, November 8, 1863; died in Scarsdale, New York, November 4, 1939; graduated in medicine from Bellevue Hospital Medical College in 1889; elected a Fellow of the Academy, March 16, 1905.

Dr. Cassell was consulting ophthalmologist to the Knickerbocker and the Manhattan Eye, Ear and Throat Hospitals. He was a Fellow of the American Medical Association and a member of the State and County Medical Societies.

CUSHING, HARVEY WILLIAMS: 789 Howard Avenue, New Haven, Connecticut; born in Cleveland, Ohio, April 8, 1869; died in New Haven, Connecticut, October 7, 1939; received degrees from Yale University, A.B., 1891, A.M. (Hon.) 1913; Sc.D., 1919; from Harvard University, A.M., M.D., 1895; Sc.D., 1931; M.D. (Hon. Causa.) Belfast, 1918; Strasbourg and Brussels, 1930; Budapest and Bern, 1931, and Paris, 1933; from Washington University, Sc.D., 1915; from Western Reserve University, LL.D., 1920; also LL.D. from Cambridge University, 1920, and Edinburgh and Glasgow Universities, 1927; and from Dartmouth College, Litt. D., 1929; elected an Honorary Fellow of the Academy November 18, 1926.

Dr. Cushing had been engaged in the practice of surgery from 1895 to 1933. He was associate professor of surgery at Johns Hopkins University, 1902-12; professor of surgery at Harvard University and surgeon-in-chief to the Peter Bent Brigham Hospital 1912-32; emeritus Sterling Professor of Neurology at Yale University and emeritus Moseley Professor of Surgery at Harvard University.

From May 1917 to March 1919, Dr. Cushing was Director of the U. S. A. Base Hospital No. 5 attached to the B. E. F. in France. He was also senior consultant in neurosurgery with the A. E. F. in 1918. The Distinguished Service Medal was awarded him by the United States Government for his work.

Dr. Cushing received the Charles Mickle Fellowship of the University of Toronto, 1922; the Cameron prize of the University of Edinburgh, 1924; and the Lister Medal (London) 1930. He was a Fellow of the American Medical Association, a Fellow of the American College of Surgeons and its president in 1923, a member of the American Neurological Association and its president in 1923, a Fellow of the American Surgical Association and its president in 1927, a Fellow of the American Academy of Arts and Sciences, an Honorary Fellow of the Royal College of Surgeons, England (1913), Ireland (1918), and Edinburgh (1927); a foreign member of the Royal Society of London, a member of the Society of Clinical Surgery, Society of Neurological Surgeons, New England Surgical Society, American Association of Neuropathologists; American Psychiatric Association, American Association of Pathologists and Bacteriologists, American Society for Experimental Pathology; National Academy of Sciences; American Physiological Society, the Massachusetts County and State Medical Societies; an associate member of the Société Royal de Bruxelles, and a corresponding member of the Société de Biologie, and Académie de Médecine (Paris) and the Medical Chirurgical Society, Edinburgh.

Dr. Cushing was the author of "The Pituitary Body and Its Disorders," 1912; "Tumors of the Nervus Acusticus," 1917; "The Life of Sir William Osler," 1925 (Pulitzer Prize); "A Classification of the Gliomata," (with P. Bailey) 1925; "Consecratio Medici and Other Essays," 1928; "Intracranial Tumors," 1932; "Pituitary Body and Hypothalamus," 1932; and various papers dealing especially with neurological surgery.

FARRAND, LIVINGSTON: Federal Hill Road, Brewster, New York; born in Newark, New Jersey, June 14, 1867; died in New York City, November 8, 1939; received the degrees of A.B. 1888, A.M. 1891 Princeton University; M.D. 1891, College of Physicians and Surgeons, Columbia University; Ph.D. (honorary) 1924, Rensselaer Polytechnic Institute; L.H.D. 1922, Hobart College; LL.D. 1924, Colorado College and University of Denver, 1917 University of Michigan, 1919 University of Colorado, 1922 Union College, Princeton University and Colgate University; 1923 Yale University; 1925 University of Pennsylvania and Dartmouth College; 1927 University of Toronto; 1929 Columbia University; 1934 Syracuse University; 1935 Lafayette College, and in 1936 Williams College; elected an Honorary Fellow of the Academy October 3, 1929.

Dr. Farrand was president of Cornell University from 1921 to 1927 and president emeritus of that institution up to the time of his death. From 1914 to 1919 he was president of the University of Colorado. He was at Columbia University as instructor of psychology, 1893-1901; assistant professor of anthropology, 1901-03; and professor of anthropology, 1903-04.

He was a Fellow of the American Association for the Advancement of Science, a Fellow of the American Medical Association, executive secretary of the National Association for the Study of Prevention of Tuberculosis, 1905-14, treasurer of the American Public Health Association, 1912-14, a member of the American Climatological Association, the American Anthropological Association and the American Psychological Association.

GAY, FREDERICK PARKER: 630 West 168 Street, New York City, born in Boston, Massachusetts, July 22, 1874; died in New York City, July 14, 1939; received his A.B. degree from Harvard in 1897; his medical degree from Johns Hopkins University in 1901 and the degree of Sc.D. from George Washington University in 1932; elected a Fellow of the Academy February 4, 1926.

Dr. Gay, who was professor of bacteriology at Columbia University from 1923 until the time of his death, was an assistant on the Johns Hopkins Medical Commission to the Philippines in 1899; assistant demonstrator of pathology at the University of Pennsylvania, and a Fellow of the Rockefeller Institute for Medical Research, 1901-03; a research student under Jules Bordet at the Pasteur Institute, Brussels, 1903-06; bacteriologist to Danvers Insane Hospital, 1906-07; instructor in pathology at Harvard Medical School 1907-10; professor of pathology at the University of California, 1910-21 and professor of bacteriology at that institution, 1921-23. During the World War he was a major in the Medical Corps, U.S.A., assigned to the Yale Army Laboratory School. Later he served on the Commission for the Relief of Belgian Education.

Dr. Gay was a member of the medical section of the National Research Council, 1912-24, its Chairman in 1922, and Chairman of the Medical Fellowship Board, 1922-25. He was exchange professor to Belgian universities in 1926. From 1932 to 1935 he was Chairman of the Scientific Advisory Board of the Leonard Wood Memorial. Dr. Gay was a fellow of the American Medical Association, the American Association for the Advancement of Science, a member of the Association of American Physicians, American Association of Pathologists and Bacteriologists, Society of Experimental Biology and Medicine, Association of American Bacteriologists and American Association of Immunologists and a commander of the Order of the Crown of Belgium. Dr. Gay's works included "Studies in Immunity," 1909; "Typhoid Fever," 1918; and "Agents of Disease and Host Resistance" (with others), 1935. He was also a contributor to scientific journals on bacteriology, immunology and pathology.

MCDONALD, DENNIS JOHN: 52 West 94 Street, New York City; born in New York City, February 10, 1865; died in Astoria, Long Island, New York, October 7, 1939; graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1888; elected a Fellow of the Academy February 6, 1902.

Dr. McDonald was consulting otolaryngologist to the Misericordia Hospital, a diplomate of the American Board of Otolaryngology, a Fellow of the American College of Surgeons and a member of the American Medical Association and the County and State Medical Societies.

SADLIER, JAMES EDGAR: 295 Mill Street, Poughkeepsie, New York; born in Walden, New York, March 28, 1865; died in Poughkeepsie, New York; October 9, 1939; graduated in medicine from the Albany Medical College in 1887; elected a Fellow of the Academy February 2, 1905.

Dr. Sadlier was one of the founders and surgeon to the St. Francis Hospital of Poughkeepsie, consulting surgeon to the Northern Dutchess Health Center at Rhinebeck and the Butterfield Memorial Hospital at Cold Springs. He was a Fellow of the American College of Surgeons, a Fellow of the American Medical Association, a diplomate of the American Board of Surgery, a member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons and a former vice-president of that Association, a member of the American Society for the Control of Cancer, a member of the National Tuberculosis Association, a member of the New York State Medical Society and one of its

former presidents, and a member of the Dutchess and Putnam County Medical Societies.

SOVAK, FRANCIS WASHINGTON: 755 Park Avenue, New York City; born in New York City, July 4, 1885; died in New York City, October 27, 1939; graduated in medicine from New York University and Bellevue Medical College in 1911; elected a Fellow of the Academy January 5, 1922.

Dr. Sovak was clinical professor of obstetrics and gynecology at New York University College of Medicine, assistant attending gynecologist to the Polyclinic Hospital, attending gynecologist to the Misericordia Hospital, and associate attending gynecologist and obstetrician to Bellevue Hospital. He was a diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, a Fellow of the American Medical Association, and a member of the County and State Medical Societies.

STEIN, SYDNEY ABRAHAM: 200 West 87 Street, New York City; born in New York City, November 22, 1867; died in New York City, September 29, 1939; received the degree of B.A. from the College of the City of New York in 1888 and graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1891; elected a Fellow of the Academy April 1, 1909. He was a Fellow of the American Medical Association and a member of the County and State Medical Societies.

STEVENSON, GEORGE: 526 West 111 Street, New York City; born in New York City, July 24, 1862; died in Mt. Morris, New York, September 11, 1939; graduated in medicine from Jefferson Medical College, Philadelphia, in 1903; elected a Fellow of the Academy November 2, 1916.

Dr. Stevenson was a Fellow of the American Medical Association, and a member of the National Society for the Advancement of Gastroenterology, the Association for Research in Nervous and Mental Disease, and the State and County Medical Societies.

WOLLSTEIN, MARTHA: 35-59 — 164 Street, Flushing, New York; born in New York City, November 21, 1868; died in New York City, September 30, 1939; graduated in medicine from the Woman's Medical College of the New York Infirmary for Women and Children in 1889; elected a Fellow of the Academy December 5, 1901.

Dr. Wollstein was pathologist to the Babies Hospital from 1892 until her retirement in 1935. She was demonstrator of histology at the Woman's Medical College, 1890-93, and demonstrator of pathology at this institution, 1893-99. In 1906, and until her resignation in 1921, Dr. Wollstein was an associate member of the Rockefeller Institute for Medical Research. She was associated with the College of Physicians and Surgeons, Columbia University, as associate in diseases of children, 1925-28; as assistant clinical professor of diseases of children, 1928-30; and as assistant professor of diseases of children and of pathology, 1930-35.

Dr. Wollstein was Chairman of the Pediatric Section of the Academy, 1933-34, and a member of the American Pediatric Society, Society of Experimental Biology and Medicine, the Harvey Society, the New York Pathological Society and the Association of Pathologists and Bacteriologists.

ZEISS, ROBERT FREDERICK: 1 East 63 Street, New York City; born in Brenham, Texas, November 21, 1892; died in New York City, August 8, 1939; graduated in medicine from the University of Texas School of Medicine in 1916; elected a Fellow of the Academy November 6, 1930.

Dr. Zeiss was consulting urologist to the United States Marine Hospital, a Fellow of the American Medical Association, a member of the American Urological Association and a member of the County and State Medical Societies.

LECTURES TO THE LAITY

1939-1940

The Fourth Series of Lectures given during the 1938-1939 season has lived up to the high standard established in the preceding series. These lectures, dealing with the history and romance of medicine, had an average attendance of five hundred at each lecture which speaks well for the enthusiasm with which these speakers were received by the lay public.

Hitherto the lectures have dealt primarily with the development, romance and philosophy of medicine. The committee in charge recognizes, from the requests made by many lecture followers, that the lay public is primarily interested in its own well-being and that of the community. With this in mind, an effort has been made to depart from historical medicine to a certain degree and to select topics which will be of more immediate and practical service.

November 30, 1939 . . . . . *The inheritance of mental disease*

ABRAHAM MYERSON

Clinical Professor of Psychiatry, Harvard Medical School

December 28, 1939 . . . . . *The ascent from Bedlam*

RICHARD H. HUTCHINGS

Emeritus Professor of Clinical Psychiatry, Syracuse University Medical College

January 25, 1940 . . . *The story of our knowledge of the blood*

PAUL REZNIKOFF

Assistant Professor of Clinical Medicine, Cornell University Medical College

February 29, 1940 . . . . . *The romance of bronchoscopy*

CHEVALIER JACKSON

Honorary Professor of Bronchoesophagology, Temple University School of Medicine

March 28, 1940 . . . . . *The story of the viruses*

THOMAS M. RIVERS

Director, The Hospital of The Rockefeller Institute for Medical Research

April 25, 1940 . . . . . *Chemical warfare against disease*

PERRIN H. LONG

Associate Professor of Medicine, Johns Hopkins University

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